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The Canadian Medical Association Journal

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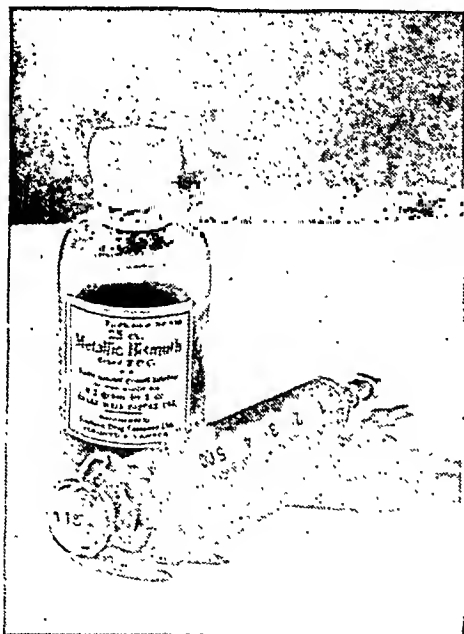
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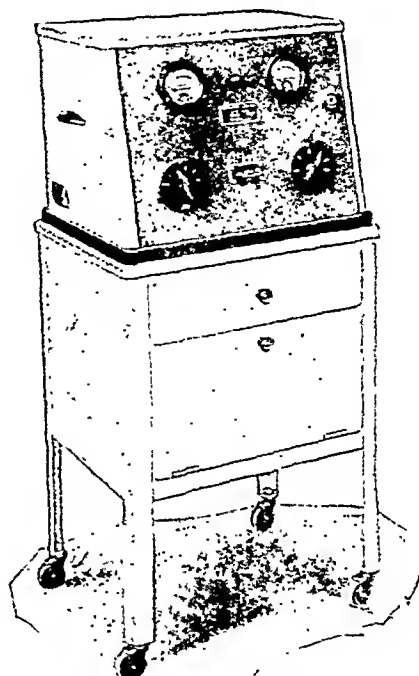
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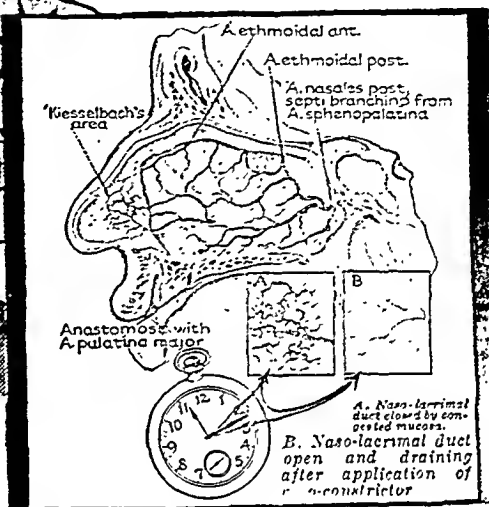
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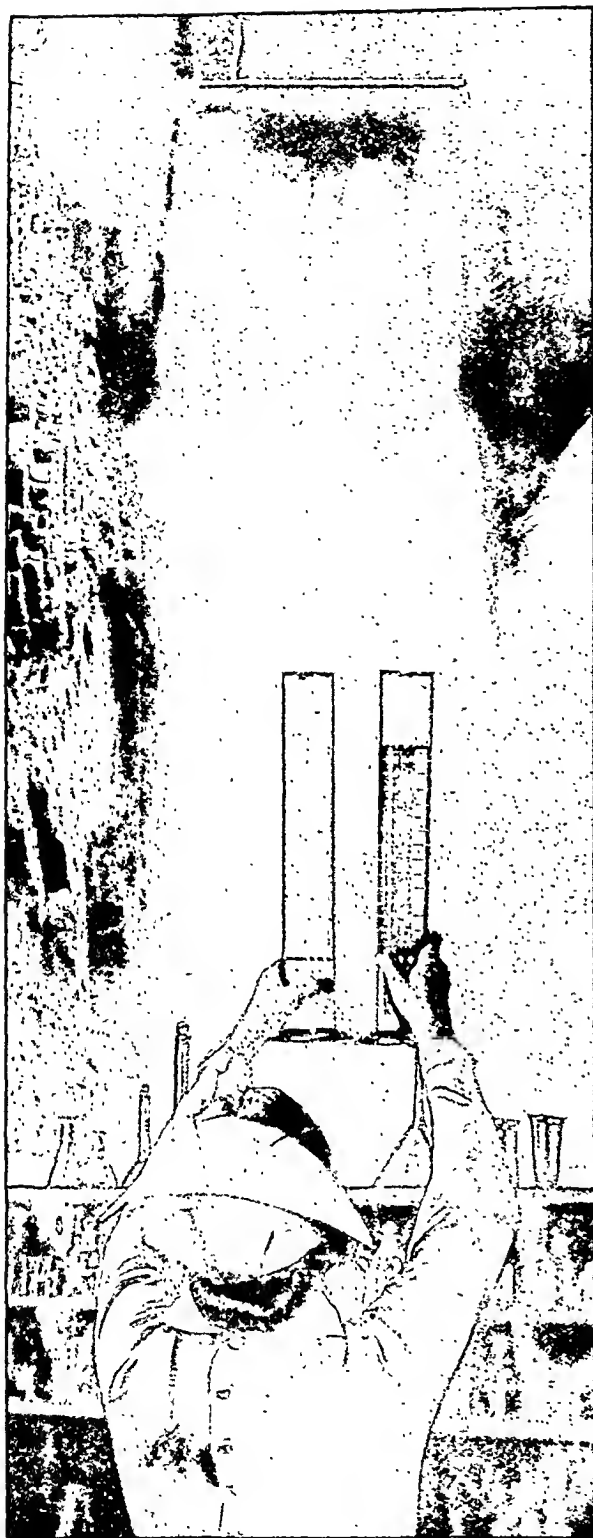
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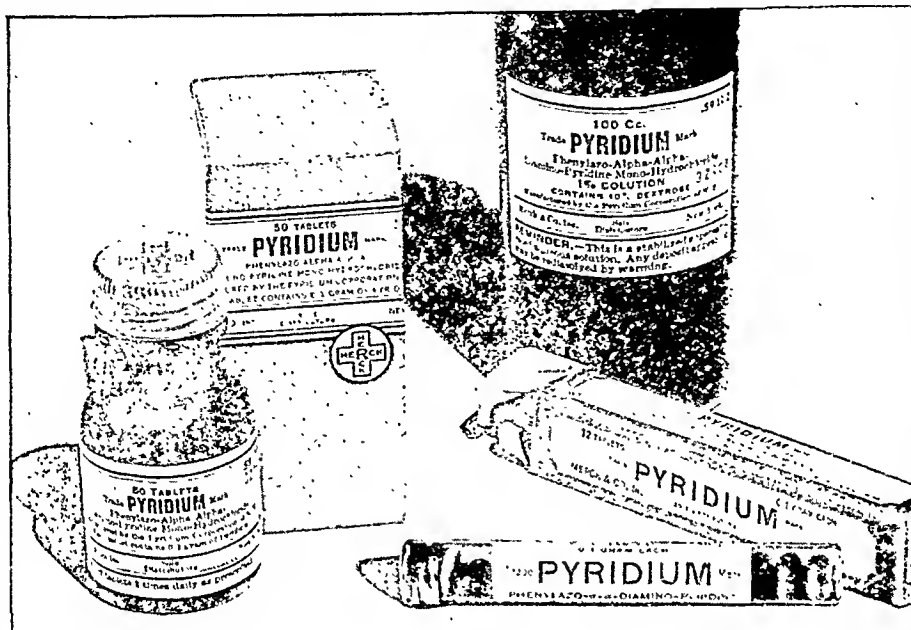
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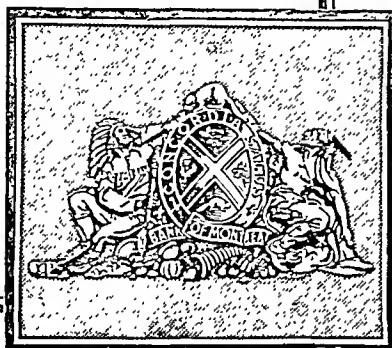
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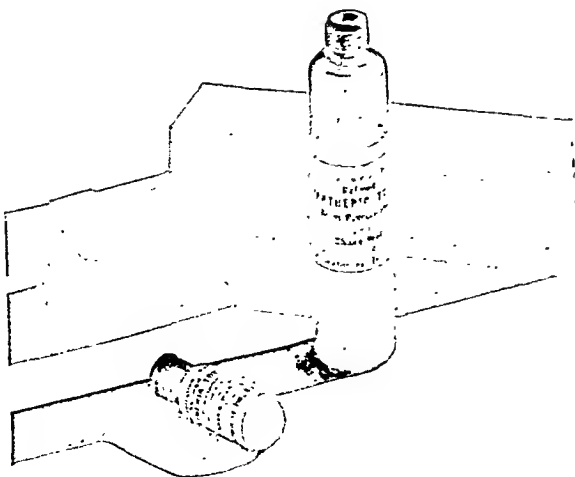
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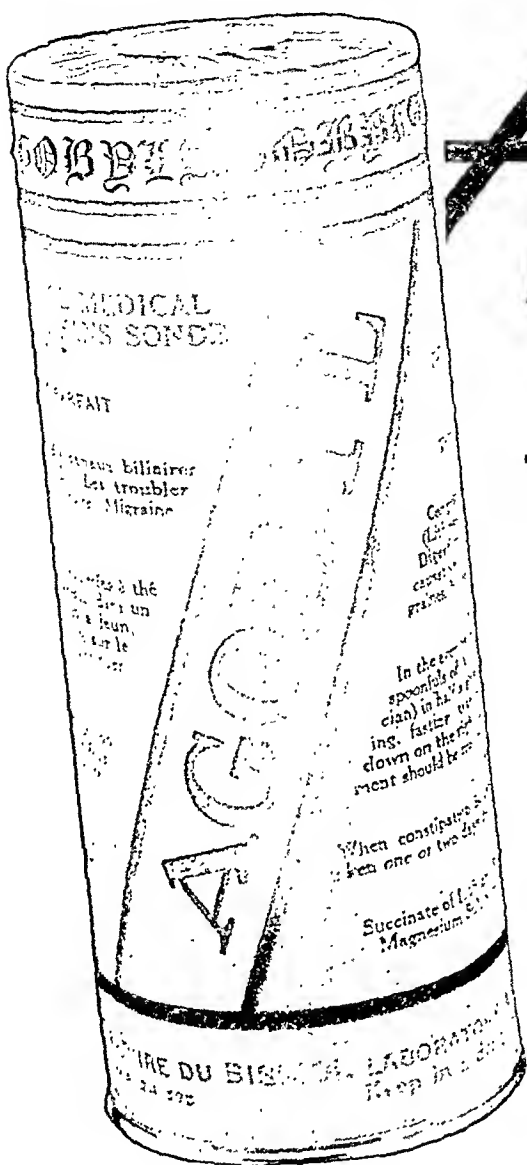


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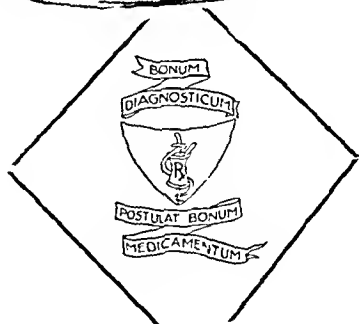
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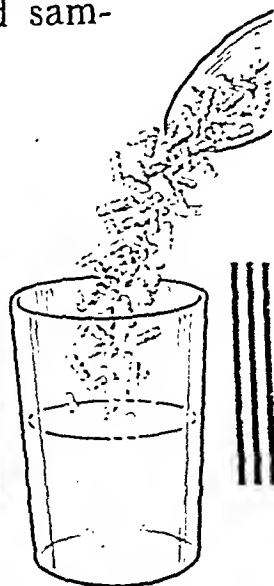
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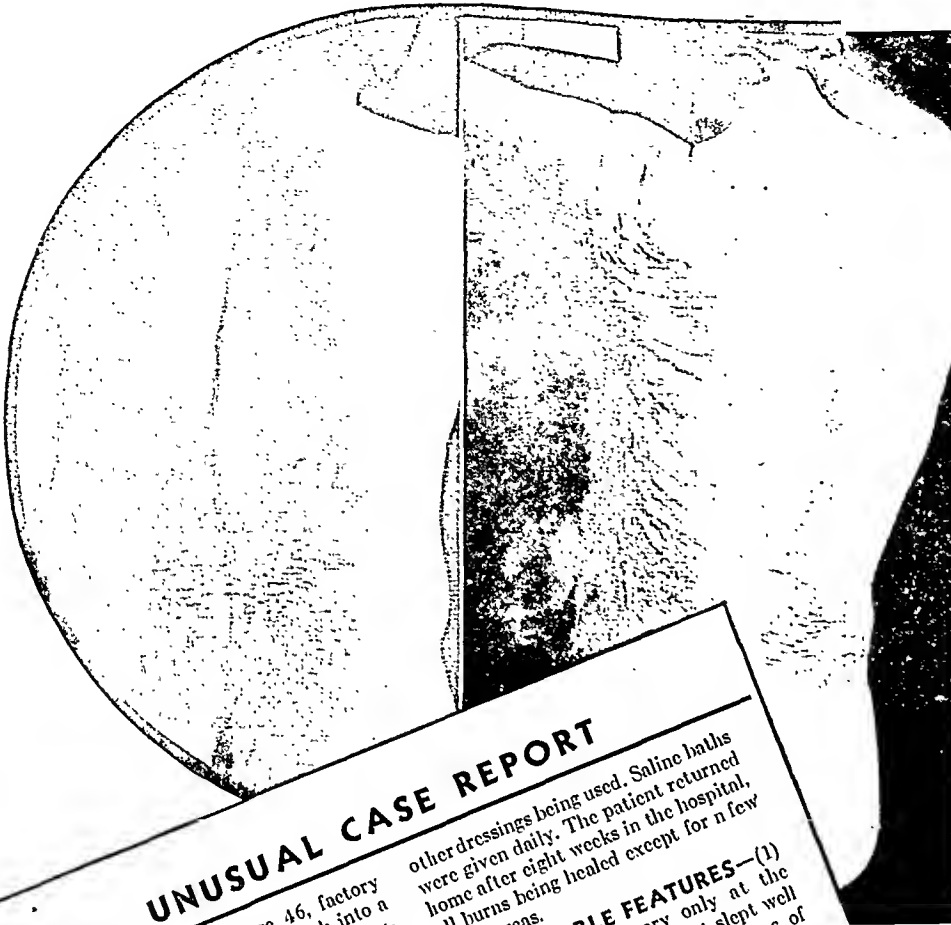
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INTERNAL SECRETION AS A FACTOR IN THE ORIGIN OF CANCER*

BY LEO LOEB, E. L. BURNS, V. SUNTZEFF AND MARIAN MOSKOP,

St. Louis, Mo.

DURING the period from 1907 to 1916 some notable additions to our knowledge of the causes of cancer were made.¹ (1) The great significance of heredity in the origin of certain tumours has been established; in particular it could be shown that different strains or families of mice kept under the same environmental conditions differ greatly in cancer incidence and that these differences remain constant in successive generations. (2) The experimental production of cancer through long-continued application of tar or through the introduction of metazoic parasites in certain organs has been accomplished. (3) It was during this period that the first experiments were carried out which definitely proved the significance of internal secretions or hormones in the development of certain cancers. We are here concerned with the effect of hormones on the development of mammary cancer in mice, but a full discussion of the various problems concerned in this condition cannot at this time be given. We can merely attempt to state briefly the principal conclusions to which these investigations have led so far.

There are two ways in which the significance of hormones in a vital process can be demon-

strated—by diminishing the quantity of active hormones or by increasing it, and by studying the effects of the deviation from the normal hormone level. Both of these methods have been applied in the case of the ovarian hormones, which are responsible for the development of mammary cancer in mice and they have led to concordant results.

By diminishing the amount of hormone action by means of ovariectomy performed at various periods of life in mice, it could be shown that a quantitative relationship exists between the quantity of hormone which has had a chance to act on a certain tissue, and the frequency with which cancer develops in a given family or strain, and the average age at which it appears. In the majority of high tumour rate strains, in which the mice had been ovariectomized at the age of three and four months, cancer was entirely prevented; in mice ovariectomized at the age of five and six months the cancer rate was definitely diminished, and the mice in which cancer appeared were older. In mice ovariectomized at the age of eight and ten months cancers appeared about as frequently as in normal mice, but the cancer age was perhaps somewhat greater.¹ These observations were confirmed and in a certain direction extended in the interesting experiments of Cori.² We may therefore conclude that the greater the quantity of ovarian hormone that has been active, the greater is the number of individuals in a certain family or strain in which mammary cancer develops and the earlier the cancerous transformation of the gland tissue occurs.

A comparison between the cancer incidence in breeding and in non-breeding mice showed the

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We are indebted for the oestrin used in these experiments to the Schering Corporation, who supplied us with Progynon-B (Benzoic-acid ester of dihydrofolliculin); and to Parke Davis Company, who furnished us with crystalline theelin (Keto-hydroxy-oestrin).

greater incidence in the breeding animals, although the degree of this difference varies in different strains; it is more significant in some than in others.³ However, in every strain removal of the action of the ovarian hormones early in life has a greater effect and usually a very much greater effect on the reduction of the cancer rate than prevention of breeding.⁴ This fact indicates that primarily œstrin, which alone is active in non-breeding mice, is concerned in the origin of mammary cancer, but that probably the lutein hormone, which is active during the state of pregnancy, and possibly also the changes which the mammary gland undergoes during the period of nursing may in addition have some influence in this respect.

Another fact that seems of great interest has been established through these investigations, namely, that if a certain quantity of hormone action has taken place the cancerous transformation occurs subsequently, even though the further action of the hormone has ceased a considerable time before the first appearance of cancer. It is therefore very likely that cancer is preceded by a preparatory period, during which changes take place in the mammary gland tissue which may not be visible under the microscope, but which cause the reactions of the tissues from then on to be such that ordinary functional and metabolic activities are able to bring about the cancerous transformation of the tissues.¹ We may then conclude that the so-called "spontaneous" mammary cancer of mice is due to the action of ovarian hormones, and the fact that different strains and families differ in regard to the number of individuals which become cancerous and in regard to the age when this change occurs shows that, in addition to the hormone action, another factor, a hereditary one, has to be considered, which differs in different strains and is characteristic of each strain.

Wherein does this hereditary factor consist? It was conceivable that there might be hereditary differences in the sexual cycles in strains with a high and with a low tumour incidence, which might lead to a greater production of œstrin in the former, and thus make possible a more intense action of ovarian hormones. However, it can be shown that while differences in the sexual cycle do exist between different strains of mice and even between different individuals belonging to the same strain, (differences which may be hereditary) there is no relation between

these differences in the cycle and the tendency of these strains to become cancerous.⁵ There remains the possibility that in different strains the readiness with which the cancerous transformation occurs differs. But the further question arises as to the stage at which the hereditary differences between different strains set in, and wherein the changes which take place in the mammary gland under the influence of the hormone leading ultimately to the cancerous transformation differ in high and low tumour-rate strains. We could show that a limited number of small or large doses of œstrin given to mice call forth the same response in high and in low tumour-rate strains, and also Gardner, Diddle, Allen and Strong found no difference when small doses were given over a somewhat longer period of time.⁶

This leads us to the second type of experiments in which the effect of an increase of hormone action over the normal level on the mammary gland has been studied. We first attempted such an increase in hormone action by transplanting ovaries into castrated males belonging to high tumour-rate strains. In the majority of cases the follicular tissue did not persist in the transplanted ovaries, and therefore the production of an excess amount of œstrin could not be expected to take place. However, by operating on a very large number (210) of male mice Murray could observe the development of tumours in 15 of them.⁷ Although occasionally cancer develops spontaneously in male mice, the appearance of tumours in these 15 animals must be attributed to the increase in hormone action. Cori attempted to raise the cancer rate in ovariectomized female mice by long continued injections of small doses of œstrin, but without success. Our microscopic examination of the mice thus treated showed that no active proliferation, such as is noticeable at the time of œstrus, occurs under these conditions. However, subsequently, Lacassagne found that by injecting very large doses (he used as much as 100 rat units of œstrin a week) it was possible to produce adenocarcinoma in the mammary gland of mice, and he showed, further, that this transformation could be induced much more readily in mice belonging to high tumour-rate strains than in those belonging to strains with a low tumour rate.⁸ The experiments on which Lacassagne bases his conclusions are convincing; they are of very great interest and importance

and have contributed much to the progress in this field.

Before we learned of the last-mentioned investigations, we had already planned to study on a larger scale than had been previously studied the effects of increased doses of ovarian hormones on the development of mammary cancer. So far we have observed the results obtained after long continued injections of œstrin in 126 mice belonging to strains differing in their normal tumour rate. We found that the number of mice in which tumours develop increases with the increase in the amount of œstrin injected, and that doses below 5 rat units a day are ineffective in this respect or at most lead only to a slight increase in certain high tumour-rate strains. Males are at least as readily accessible to the cancerous transformation of the mammary gland as are non-breeding females, an observation which agrees with the findings of Lacassagne. We also found that mammary cancer is produced more readily in high than in low tumour-strains. This increase in the rate of mammary carcinoma can be demonstrated not only in males but also in non-breeding females; however, we have so far not succeeded in raising the cancer rate here much above the incidence observed in breeding females of the same strain. We could raise it perhaps somewhat above that level by injecting œstrin into mice belonging to high tumour-rate strains which had been allowed to breed once or several times, but the effects in this respect are so small that we cannot as yet consider them as definite. On the other hand, ligation of the galactophorous ducts in mice injected with œstrin in our experiments did not increase the tumour rate over that observed in non-ligated mammary glands, a result which might have been foreseen, because the product of secretion in mammary glands of mice injected with larger doses of œstrin is retained also in cases in which the ducts have not been ligated.

Under the influence of the long-continued action of œstrin, there develop gradually, step by step, lobules of mammary gland tissue consisting of rather large acini. The cells composing these acini have much cytoplasm, their nucleus is vesicular and often has one central large nucleolus. These acini may show secretion, as is indicated by the appearance of intracellular vacuoles of different sizes and varying number. The secretion may be very active. But if further growth stimuli reach these cells, in-

stead of secreting, they proliferate actively by mitosis and also amitoses and hypertrophic nuclei may be seen; the tubules which thus develop often coil around in an irregular manner. This is the usual beginning of tumour formation. Such large-celled tissue, which readily undergoes either secretion or proliferation, may be considered as precancerous, although as long as it merely secretes and is not spurred on by further growth stimuli it may not represent as yet a real cancer. This is the most frequent change which initiates carcinomatous transformation, although in rare instances other changes, such as the cancerous proliferation of the epithelium of large ducts, may occur. The precancerous tissue appears first in isolated places, but with progressive stimulation it extends to wider areas, and in the end may become almost general. If in this tissue a true carcinoma develops it appears first in one spot, but with the progress of stimulation another spot may become similarly affected, and in the end multiple tumours develop. As the endpoint of these stimulations a generalized transformation of the mammary gland tissue into carcinoma may be foreseen. As stated, intermediate stages in the development of this precancerous tissue occur, and the rapidity of this transformation depends upon the intensity of the stimulation and on the reactivity of the tissue as determined by hereditary factors. The description of beginning spontaneous cancer in the mammary gland of the mouse by Apolant agrees with our observations in the experimentally produced cancer, and we have also observed the same changes in spontaneous mammary cancer. Also Lacassagne has seen acinar tissue in which secretion appears and in which carcinoma develops.

While there is, as stated, no difference in the early reactions of mice belonging to high and low tumour-rate strains, as far as the readiness with which the mammary gland and also the vagina and uterus respond to œstrin is concerned, the readiness with which the later changes take place seems to differ in high and low tumour-rate strains. As to the ovary, we have not observed differences in regard to the formation of corpora lutea in high and low tumour-rate strains; but we have noted that after long-continued action of large doses of œstrin corpus luteum formation in the ovaries seems to cease, although the follicles may continue to grow to large size.

If we compare the frequency of mammary cancer in breeding and in non-breeding mice belonging to high and low tumour-rate strains, and, further, if we compare the response of non-breeding mice to large doses of œstrin in these strains, we find threshold differences in the response of these various families and strains to these stimuli. Some strains which possess a high tumour rate under conditions of breeding and a low rate under conditions of non-breeding, are in the non-breeding state near the threshold which tends to cancerous transformation. The small stimulus added by breeding is all that is required for the realization of this tendency. In other high tumour rate strains the stimulation by œstrin which takes place in the course of the normal cycle causes almost the maximum response, and the stimulus acting on the mammary gland during pregnancy, and perhaps also during lactation, can be only a relatively unimportant added stimulation. In certain low tumour-rate strains there is a response to neither of these stimulations. Various other combinations may occur in strains with an intermediate tumour incidence.

We have attempted to express the relation which exists between the effect of the hereditary tendency to cancer and the stimulating action of hormones or other factors by the equation $H \times S = C$, in which H means the constitutional condition of the tissue, S the quantity of stimuli, and C the resulting cancerous transformation.⁹ This equation holds good in a general way within a certain range of the action of these factors. However there exists the difficulty that, while we can determine at least in an approximate manner the quantity of the stimuli which has been active, our determination of the zero point of hereditary tendency is arbitrary. Even between those strains in which cancer has not been observed so far differences in the tendency to cancer may still exist. There is a further difficulty which concerns the hereditary tendency to cancer within a certain strain. Theoretically, the behaviour of all individuals belonging to strains which have been propagated through very many generations by brother-sister matings should be the same, inasmuch as a homozygous condition would be expected to prevail in such a strain; but actually we find very great differences in the reactions to the same stimuli on the part of different individuals belonging to the same family or strain. It is usually assumed that these individual dif-

ferences are due to variable environmental factors. However it is difficult to understand why random variations in environmental conditions should make possible a constancy in the averages of tumour incidence and tumour age in successive generations of mice belonging to the same inbred strain. We have therefore to consider the possibility that gradually through mutation or otherwise differences develop again between individuals in the same closely inbred strain and that the averages of these changes are constant.

Estrogenic hormones act not only on the mammary gland; they cause marked growth processes also in the epithelium of the vagina and less marked changes in the uterus. The prolonged injection of large doses of œstrin is not without specific effects on these organs, for we have observed that it affects both in the same direction as it does the mammary gland. But it is particularly the upper portion of the vagina which in the course of time undergoes changes. The epithelium begins to send irregular processes into the connective tissue, and in the end pictures not unlike those seen in beginning squamous cell carcinoma may appear. However on purely morphological grounds it is unsafe to characterize these conditions as representing already a complete cancerous transformation; we may have to deal with earlier, still reversible stages in this process. The same restriction holds good also in the case of the experiments of Overholser and Allen, who observed that injections of œstrin and corpus luteum hormone into monkeys whose cervix of the uterus had been injured induced an atypical growth of the epithelium.¹⁰ A downgrowth of squamous epithelium of the vagina along the cervical glands took place. Also in the uterus abnormal growth processes of various kinds have been observed and in a few of these a metaplasia of the cylindrical epithelium into squamous epithelium has been seen by us similar to the change noted by Selye, Thomson and Collip.¹¹ In other instances a downgrowth of the uterine glands into or through the muscle tissue has been noted. It is especially the junction between cervix and uterus in which the epithelium tends to an abnormal downgrowth into the connective tissue. In the uterus, as well as in the vagina, as a result of the continuous stimulation by œstrin the epithelium begins to grow in an abnormal direction. Particularly in the upper part of the

vagina we can follow the thickening and down-growth of the surface epithelium into the connective tissue. At first the squamous epithelium becomes merely thickened, but this condition is followed by the formation of small papillae reaching downward, and, step by step, these papillae penetrate deeper while at the same time they become more and more irregular. We have therefore to deal with a response of the epithelium graded in degree in accordance with the intensity of the stimulation which had been applied. Further, in two instances the frequently repeated injections of œstrin led to the production of spindle-cell sarcoma at the point of insertion of the needle, both tumours appearing in other than the high tumour-rate strains; in these cases it is more probable that the trauma, as such, rather than the œstrin, was responsible for the results.

While so far the significance of internal secretions in the production of cancer has been definitely demonstrated only in the case of mammary carcinoma in mice, it is very probable that internal secretions likewise play a rôle in the cancerous transformation of normal tissues in all those cases in which tissues are normally stimulated in their growth processes by certain hormones. These effects may in some instances be of primary significance, while in other cases internal secretions may play only the rôle of secondary factors intensifying the action of other stimulating agents. The recent experiments of Bagg,¹² who observed that injections of extract of anterior pituitary gland of sheep prolongs the time of the year during which a teratoma testis can be produced in adult roosters by means of injection of zinc chloride into this organ, would represent an example of the second kind of action. It may be expected that ovarian hormones play an etiological rôle also in uterine and vaginal cancer and anterior pituitary hormones may perhaps be concerned in certain cancers of the thyroid gland and of other tissues.

There is another line of observations which may possibly have some bearing on this question. Laqueur and his associates, as well as P. Engel, have found that in man and animals which are bearers of rapidly growing tumours œstrin or œstrogenic substances may appear in the blood.^{13, 14} This applies even in cases of transplanted tumours, sarcoma as well as carcinoma in mice. Loewe, Raudenbush and Voss¹⁵ noted an increased amount of œstrin in the tissue of human tumours

which originated in the stomach, liver and other organs. Zéphiroff and Dobrovolskaia-Zavadskaia¹⁶ obtained an œstrogenic substance from adenocarcinomas of mice, but failed to find it in human breast carcinoma and in the normal mammary gland of the cow. More recently Geschiekter *et al.*¹⁷ have noted increased amounts of œstrin in the human breast tissue in cases of gynæcomastia, virginal hypertrophy and fibroadenoma. At present, however, it is not possible, to conclude that the presence of œstrin in these tissues indicates the existence of an etiological relationship between the hormone and the abnormal growth. The same consideration applies to the observations of B. Zondek¹⁸ who found Prolan A in the urine of persons with either genital or extragenital tumours, and also to the findings of Ferguson¹⁹ who noted an increased amount of Prolan A in the urine of men suffering from teratoma testis or from other rapidly growing tumours of this organ. These observations likewise do not permit any conclusion as to the significance of internal secretion in the origin of these tumours.

Hormones, like carcinogenic hydrocarbons and other carcinogenic agents, produce cancer by inducing often repeated or long-continued growth processes which end with the change of the tissue to a new equilibrium. All the factors which induce a cancerous transformation of normal tissues seem to have in common this property of stimulating growth, and the constant or often repeated stimulation of growth in an at first normal tissue appears to be an essential factor in the cancerous transformation. Hormones differ from certain other agents in that they affect those tissues alone on which they act also under normal conditions, while the majority of other factors may affect indiscriminately many tissues with which they come into contact. This applies to the substances which are the active carcinogenic constituents of tar, as well as to other agents, physical or chemical, which all directly or indirectly exert a stimulating effect on tissues ultimately leading to the development of cancer. However, hormones act on tissues in a specific way under normal conditions: they cause the cancerous transformations essentially by stimulating the growth of tissues to which they are specifically related, and they do not in a noticeable manner cause primarily injury to the tissue which ultimately is stimulated. Here we have to deal with a direct and primary

stimulation. On the other hand, the other kinds of substances, which are strange to the organism, may injure the stroma which supports the epithelial surface, and these secondary changes may complicate the action of these substances and add regenerative processes to a primary stimulation. Very careful microscopic examinations of the mammary gland also during the preparatory period of mice which were being injected with œstrin show that these hormones exert a direct stimulating action on the tissues, which ends with the formation of cancer. It is one of the distinctive features in the production of cancer by hormones that in this case we have to deal with agents normally adapted to the body which do not induce at the same time injury and inflammatory reactions in the underlying areas. As to the phase in the growth process in which these different agents combine with the tissues and alter them no definite statement can be made; this phase may vary in the case of different agents, just as the varying hereditary constitution of the tissues which make the latter responsive to the stimuli eventuating in cancer formation is not the same in the case of different agents, such as tar and hormones.

As we have pointed out on various previous occasions, it may be assumed that as a result of the long-continued action of growth-promoting agencies, an increased production of growth stimulating substances is gradually induced in the affected cells themselves by means of a mechanism which resembles autocatalysis, in which cyclic metabolic processes taking place in the cell automatically lead to the constant new-formation of the growth-stimulating substances.²⁰ Under certain conditions these substances may also have the effect of organizers modifying the nature of the tissues.²¹ As to the chemical nature of these substances we do not possess any definite information. More recently, when it was found that the carcinogenic hydrocarbons of tar as well as the œstrogenic substances are related to cholesterol, Cook *et al.*²² suggested that a specific carcinogenic substance, likewise a derivative of cholesterol, might be formed in the stimulated cells. However, if we consider the fact that a multitude of agents very divergent in nature may act in a similar way to these hydrocarbons, there is no necessity for thus limiting the chemical constitution of the substances developing or increased in quantity in cells, as the result of often repeated growth stimulation, and

constantly newly formed, due to processes resembling autocatalysis. A second possible interpretation would be that the growth processes taking place in the various tissues enable extrinsic filtrable agents to fix themselves on the tissues and then to induce the cancerous transformation of these tissues. However the fact that the change from the normal to the cancerous cell equilibrium is a gradual one, taking place step by step, each step leading to more intense growth processes and affecting wider and wider areas, seems to be more in accord with the first than with the second interpretation. The latter view does not exclude however the possibility that in certain cases also an extrinsic virus may furnish the stimulus to cancerous growth.

Various strains, families and individuals differ not only in the readiness with which the development of the large-celled secreting tissue, which is so readily transformed into cancerous tissue, takes place, but they differ also in other respects, such as the peculiarities of the sexual cycle and the kind of tissue which most readily responds to stimulation with the change from the normal to the cancerous cell equilibrium. There are also indications that the reaction of the surrounding connective-tissue stroma to the hyperactivity of the epithelium differs constitutionally in different strains. However the fact that such differences happen to occur in a given case between a high and a low tumour-rate strain, does not necessarily mean that these constitutional variations are correlated with the tendency towards the development of cancer in a given strain; on the contrary, a comparison of a larger number of high and low tumour-rate strains may show that these particular characteristics in a family, strain, or individual represent really independent entities which in different strains may appear in different combinations. These inherent differences in the mode of reaction of a certain tissue, together with the kind and strength of the stimulus, determine the kind of cancerous reaction which will take place under given conditions.

In a general way, and tentatively, we may conceive of three different states through which cells and tissues may pass in succession: (1) The embryonal state, in which as a result of constitutional factors inherent in cells and under the influence of organizers (contact substances), multiplication and differentiation of cells take place; (2) the more or less differentiated state

of the adult animal, in which, in accordance with the inherent characteristics of the cells, more or less specific stimuli acting within a certain range of intensity and frequency cause metabolic, functional and growth reactions, which as to intensity and nature are limited by inherent factors; and (3) the cancerous state occurring in embryonal or adult cells, which have not exceeded a certain degree of differentiation and have not as yet lost their power of propagation. In this state the organization and correlation with neighbouring tissues which developed during the embryonal state, and which in the adult state depend partly at least upon the action of contact substances and hormones, are partly lost, the intensity of propagation is increased and also certain metabolic deviations from the normal conditions have taken place. The third state is induced by stimuli acting with excessive intensity and frequency. The rapidity and readiness with which the transition to the cancerous state occurs again is determined by inherent constitutional (hereditary) characteristics of the cells. In certain cases substances or agents of a very specific nature may induce the cancerous state acutely, without the interference of preparatory stages through which the cells must first pass under usual conditions.

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TREATMENT OF ACNE ROSACEA.—Lise Carlu has obtained rapid results in the treatment of acne rosacea by a combination of the usual methods employed—namely, irradiation with erythematous doses of ultra-violet rays for the seborrhœa, electro-coagulation for the nodules and telangiectases, and massage for the erythema and seborrhœic recurrences. Electro-coagulation of the deep nodules is very efficacious: this procedure promotes

drainage which cleanses the skin very rapidly. It acts more quickly than electrolysis, and gives as good æsthetic results. Massage also aids in expressing the contents of the sebaceous glands. A case is recorded in which complete cure resulted from this treatment in a month. In this patient an appropriate diet, opotherapy, and applications of a sulphur ointment were employed as adjuvant measures.—*Bull. Soc. Franç. de Derm. et de Syph.*, February, 1936, p. 433. Abs. in *Brit. M. J.*

OBSERVATIONS ON THE ACTION OF PROTAMINE AND INSULIN IN THE TREATMENT OF DIABETES MELLITUS*

BY I. M. RABINOWITCH, A. F. FOWLER AND A. C. CORCORAN,

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HAGEDORN, Jensen, Krarup and Wodstrup^{1, 2} have shown that by combining insulin with protamine the action of the insulin is prolonged, due to the slow rate at which the insulin is liberated from this combination in the subcutaneous tissues. With the aid of the Sandison-Clark chamber inserted into rabbits' ears, Beecher and Krogh³ found that whereas, except for very small traces, regular insulin when injected practically disappeared from the lymphatics within forty-five minutes, appreciable traces of the protamine-insulin particles were still observed as late as five hours after the injection.

Aside from the more uniform action which enables the diabetic to live under more normal conditions, protamine-insulin represents a definite advance in the treatment of diabetes because of its ability to control the disease in the "insulin waster". Except for a few hours daily, the urines of these patients are rarely free of sugar, and attempts to control the glycosuria by increasing the quantity of insulin result, as a rule, in severe hypoglycæmic reactions. Failure, however, to control the glycosuria exposes these patients to the variety of complications of uncontrolled diabetes. Insulin is now obtained in much purer form than in the past, but as Kerr, Best, Campbell and Fletcher⁴ have pointed out, though increased purity has decreased the incidence of local tissue reactions, it has not enhanced its action. Many attempts have, therefore, been made to overcome this condition. In this Clinic administration of the insulin in small amounts at frequent intervals, rather than in relationship to meals, has been fairly successful in an appreciable number of cases, but the results have not been uniform. Other workers have attempted to slow the rate at which the insulin is absorbed from its site of injection. For this purpose the insulin has been ad-

ministered in mechanical mixtures (semi-solid fats, oils, lecithin, gum arabic, etc.) in combination with vaso-constrictors and with protein precipitants, particularly metallic salts. Many of these attempts have been abandoned. A number suggest that much is yet to be expected from insulin. The Danish product protamine-insulin, is, however, the first which has proved uniformly successful clinically. Practically all of the clinical experiences with protamine-insulin reported by its Danish discoverers have been repeatedly confirmed.^{4, 5, 6, 7, 8}

Except for the Danish workers, no one as yet has had a very extended experience with this product, and, because of its newness, a variety of methods have been attempted in its use. In their studies, Hagedorn *et al.* used fairly high fat diets; since their average diet consisted of, approximately, 100 grams of carbohydrate and 70 grams of protein, and since the average food value was 2,300 calories, the average daily allowance of fat was, approximately, 180 grams. With this diet, the best results were obtained by distributing the carbohydrates irregularly, that is, about 40 per cent of the total allowance at breakfast, 40 per cent at the noon meal, and 20 per cent at the evening meal. The blood sugar was also kept under better control by using the regular insulin during the day and the protamine-insulin to control the metabolism during the night. From published data the Toronto diets are still low in carbohydrate and high in fat and, though the diets in Joslin's clinic are more liberal with respect to carbohydrates, the amounts allowed are not, as a rule, as high as in our own diets. The average amount of fat is higher, namely, about 90 grams. A more recent report, however, from the Boston clinic shows that attempts have been made to use protamine-insulin with diets of much higher carbohydrate content.⁸ Wilder⁷ has also attempted to use a variety of diets with protamine-insulin. All workers have followed the Danish practice of using the regular insulin during the day and the protamine-insulin to control the carbohydrate metabolism during the night. More recent re-

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The protamine-insulin used in this study was manufactured in the Connaught Laboratories of the University of Toronto, and supplied for this work gratuitously through the kindness of Prof. C. H. Best.

ports, however, show that attempts have been made to reverse the procedure, that is, to administer the protamine product in the morning and the regular insulin later in the day. Attempts have also been made in some cases to use the protamine-insulin only. Severe and unpredictable reactions have been reported with this new insulin compound, and some of the experiences appear to have been sufficiently disturbing to warrant editorial comment.⁹

THE HIGH CARBOHYDRATE-LOW CALORIE DIET AND PROTAMINE-INSULIN

In our attempts to evaluate protamine-insulin, it was considered advisable to investigate intensively one type of diet at a time in a large number of cases. Since the high carbohydrate-low calorie diet is the diet of choice in this Clinic, our first studies were concerned with it, and the following is a summary of our experiences.

In our early experiments, and in accord with the original investigators, we also used the regular insulin during the day and the protamine-insulin during the night. With this method we also observed a number of very severe reactions characterized by slow onset and recurrence in spite of treatment. As will presently be shown, however, these reactions are avoidable by using the protamine compound only. We also have the impression that it is necessary to permit the protamine-insulin mixture to age for a number of days before it is used. When freshly prepared there is still a small amount of free insulin in the supernatant fluid. This is negligible. An appreciable amount is, however, apparently adsorbed on to, rather than chemically bound with, the precipitate. Incomplete precipitation of the insulin with the protamine is also sug-

gested from the difficulty at times of obtaining a watery clear supernatant fluid in spite of centrifuging the material at high speed; though the major portion of the protamine-insulin is in the precipitate, there is an appreciable amount in colloidal suspension. Early supplies of the protamine-insulin were accompanied by instructions to discard material which had been mixed more than ten days. We now no more use the mixture until it is at least five days old and, contrary to the general impression, protamine-insulin, as will be shown presently, is stable for months, even after exposure constantly to room temperature. In Table I are recorded stability tests of protamine-insulin which varied in age from 16 to 136 days, and it will be observed that there was no suggestion of deterioration of the mixture in any of the tests.* Because of these findings consideration was given to the possibility that the decrease of blood sugar alone following administration of the protamine-insulin mixture may be no indication of stability. There was the possibility that the protamine portion may have alone disintegrated and that the lowering of the blood sugar was due to uncombined insulin. An attempt was made to exclude this possibility by comparing the effects of a recently prepared product (2 days old) with that of a mixture 115 days old, by testing both in the same individual. The results of one such experiment (2870/36) are shown in Table II and it will be observed that the effects of the two mixtures were practically identical. The clinical experiences, in general, also clearly show the prolonged action of the protamine-insulin in

* A recent test showed that material prepared on January 31st was still very active. The mixture is, therefore, stable for at least 6 months.

TABLE I.
BLOOD SUGAR TIME CURVES FOLLOWING ADMINISTRATION OF 50 UNITS PROTAMINE-INSULIN
SHOWING STABILITIES OF MIXTURES OF DIFFERENT AGES

Subject	Jev	Web	And	J	2192/36	3847/35	406/36	1897/36	Ab	2314/36	2870/36	2876/36
Age of Mixture (Days)	16	16	22	22	30	50	44	44	65	95*	115	136
Blood Sugar:												
Before	0.125	0.107	0.080	0.106	0.116	0.172	0.185	0.277	0.215	0.277	0.208	0.333
2 hours after			0.042	0.084								
3 " "					0.099	0.103	0.113	0.357	0.057	0.200	0.131	0.263
4 " "			0.065	0.087								
6 " "	0.071	0.077		0.082	0.096	0.087	0.095	0.277	0.053	0.181	0.046	0.057
8 " "				0.068								
9 " "					0.101	0.068	0.090	0.104				

*12 units of protamine-insulin only available for this test.

spite of long exposure to room temperature. Supplies of protamine-insulin are now accompanied with the instruction that "the material should not be used after having been mixed for 14 days or longer". This slight increase in the time allowed is, however, not because of instability of the mixture, but because of the danger of contamination when used by patients. (Personal communication).

TABLE II.

BLOOD SUGAR TIME CURVES OBTAINED ON THE SAME SUBJECT WITH RECENTLY PREPARED PROTAMINE-INSULIN AND A MIXTURE 115 DAYS OLD

		Age of Mixture	
		2 days	115 days
Blood Sugar:	Fasting state.....	0.172	0.208
	3 hours after.....	0.100	0.131
	6 " ".....	0.054	0.046

ABSENCE OF REACTIONS

In all of the above tests and in the clinical work in general during our early experiments we were impressed with the large amounts of insulin which were tolerated without reactions. In each of the tests of stability shown in Tables I and II, the dosage with one exception only (2314/36) was 50 units. The few reactions which were observed were very slight. None required any treatment; recovery was spontaneous.

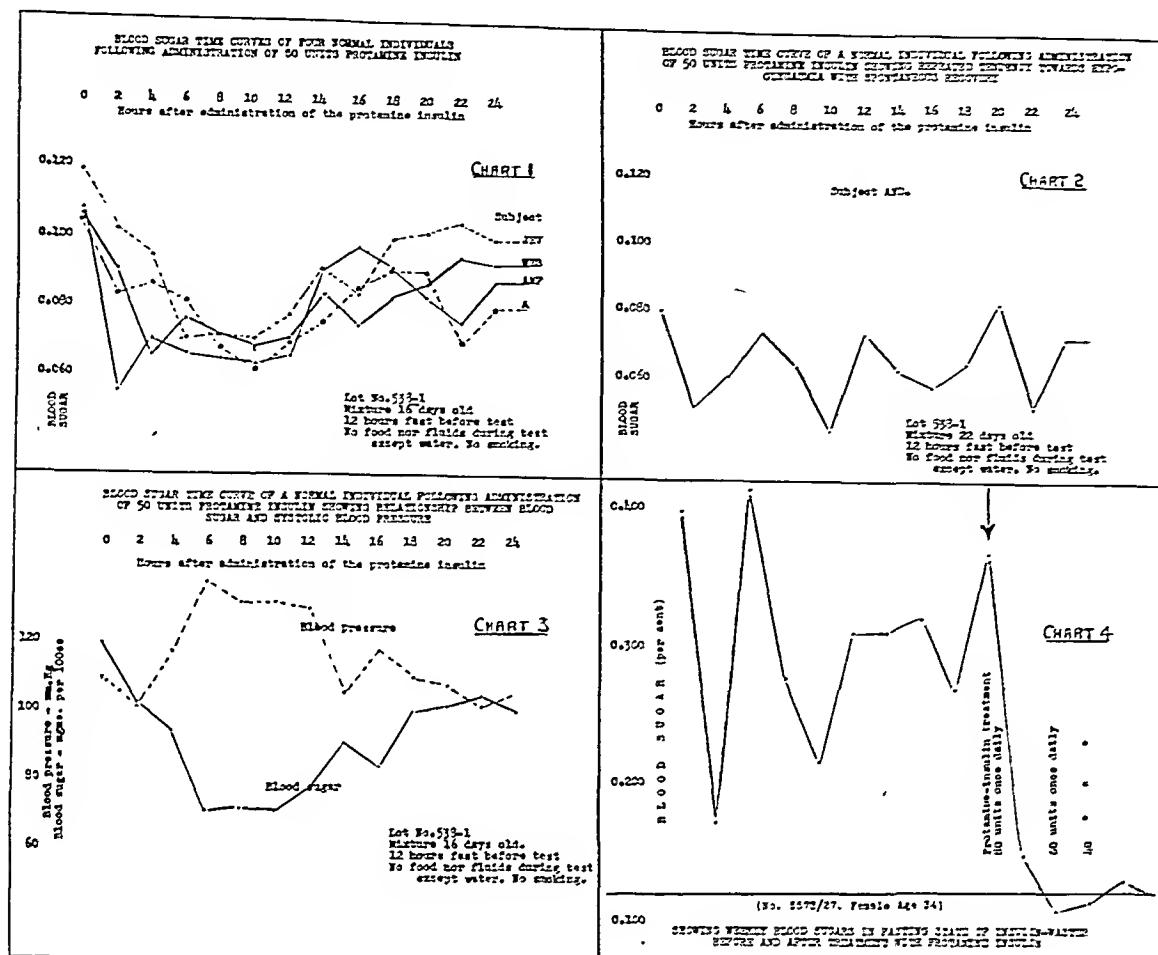
In seeking for the cause of the absence of reactions our attention was first drawn to the fact that none of the patients who tolerated these large doses of protamine-insulin mixture had been treated with both types of insulin at the same time. The picture was not, however, clear. Firstly, very severe diabetics only were used for this study; secondly, the diets were rich in carbohydrate and, thirdly, with the high carbohydrate-low caloric diet the food is not divided evenly into three meals; some food is allowed between meals and also before bed-time. That the severity of the diabetes was not alone the explanation was clearly shown by the fact that these patients were unable to tolerate much smaller quantities of the regular insulin; and that the diets were not the cause was shown by our experiences with non-diabetics. In Chart 1 are graphically recorded blood sugar time curves of four perfectly normal persons (medical students). In each case, the subject was allowed no food or fluids of any kind, except water, for

twelve hours before the test. A blood sugar determination was made before and then every two hours after the administration of 50 units of protamine-insulin, for the following twenty-four hours. No food or fluids of any kind, except water, were allowed until the test was completed. In view of its possible hyperglycæmic effects, smoking was also forbidden.

It will be observed that the protamine-insulin lowered the blood sugar in each case, yet none of these students developed any severe reactions; three had no signs or symptoms whatever suggestive of the disturbance; one had slight circumoral pallor and slight "nervousness" which disappeared without any treatment.

The explanation of the above findings is suggested from the experiences in other cases. In Chart 2 is graphically recorded a blood sugar time curve of another normal person (medical student), and it will be observed that the curve is not as regular as those shown in Chart 1. This curve clearly shows that as soon as the blood sugar reached the hypoglycæmic level some mechanism came into play spontaneously and caused the blood sugar to return to the normal level. The interpretation of this curve at the time was that the fluctuations were due to a disproportion between the action of adrenalin and that of the protamine-insulin. With regular insulin, when the hypoglycæmic level is reached, adrenalin is liberated, but, though it leads to mobilization of glycogen, the increase of blood sugar due to the latter is not as marked as the lowering of the blood sugar owing to the relatively large amount of circulating insulin; whereas, with protamine-insulin, owing to the slow rate at which the insulin is liberated from its combination with the protamine, when the hypoglycæmic level is reached and adrenalin is liberated, the action of the latter is greater than that of the circulating insulin.

That liberation of adrenalin is probably the correct explanation is suggested from Chart 3, in which are graphically recorded determinations of blood sugar and systolic blood pressure in one of the subjects shown in Chart 1. It will be observed that, in general, an inverse relationship was found between the blood sugar and the blood pressure. Space does not permit recording other data, but of three such tests, two showed this inverse relationship. In the third case the findings were not so definite. The fact of practical importance revealed in all of the



curves is that, though deprived of smoking and foods and fluids of any kind, except water, for 12 hours before, and 24 hours after, *perfectly normal persons were able to tolerate 50 units of protamine-insulin without severe reactions*, and it was this finding which led to the treatment of our diabetics with large single doses of the mixture.

As stated, to put the protamine-insulin to a severe test, severe diabetics only were used for this study. The vagaries of the reaction of the diabetic to diet and insulin are many, and unless the cases are carefully selected it is impossible to interpret the results of any new form of treatment correctly. Clinical impressions, though a guide to some extent, are rarely reliable unless the diabetes is very severe. In the interpretation of insulin dosage, consideration must also be given to the possibility of the presence of a complication which, when controlled, may *per se* lead to reduction of insulin dosage. It is, thus, necessary to differentiate between permanently

severe diabetes and that made temporarily severe by the complication. For these reasons a careful history was obtained and careful physical examination was made in every case before the protamine-insulin was used, and, for the same reason, we did not investigate new patients; none had been under observation for less than three years and none had less than 25 blood sugar determinations since the diet and insulin dosage were first established. As the methods used in this clinic for determining the severity of the disease and the insulin dosage have been reported elsewhere¹⁰ they will not be dealt with here.

AMOUNT OF PROTAMINE REQUIRED

From the combined experiences, our data indicate that, with the high carbohydrate-low calorie diet at least, the diabetic can be kept under reasonably good control with one daily injection of protamine-insulin in most cases; and, provided the mixture is permitted to age

properly, we have found no reason to fear the large doses which are necessary. Space does not permit citation of all of the experiences in detail. The best example of the effectiveness of a single large dose is found in experiences with "insulin-wasters". The finding of one such case is graphically recorded in Chart 4. In this graph is recorded the weekly blood sugars obtained in the fasting state since the institution of treatment with protamine-insulin and, for purposes of comparison, the last ten blood sugars observed before this treatment. This graph clearly shows that even in the "insulin-waster", in spite of wide oscillation of the blood sugars, one large single dose of protamine-insulin may be effective.

In Table III are recorded the large dosages of protamine-insulin used to date, their incidence, and the corresponding number of reactions. It will be observed that there were very few of the latter. None has had a severe reaction as yet; a feeling of "uneasiness" has been the only complaint, except in three cases, and in these the reactions were readily controlled with the juice of one orange. These clinical experiences fit in with those of Best. Depancreatized dogs are being kept alive and in good health in the Toronto laboratories with large doses of protamine-insulin once a day (personal communication).

A number of our patients are being treated at home and report for blood sugar determinations once a week. In the interpretation of the above results, it is, therefore, important to consider the possibility that the few reactions may have been due to high blood sugars when the protamine-insulin was administered. That this, however, is not the explanation is suggested from Table IV in which are recorded dosages of protamine-insulin, their incidences, and the corresponding number of reactions, when the fasting blood sugars were known to be perfectly normal in these cases before administration of the protamine-insulin. It will be observed that two reactions only were encountered with as many as thirty-two injections of protamine-insulin, ranging between 60 and 140 units.

The graph shown in Chart 4 does not, of course, indicate the immediate effects of treatment, since it represents weekly blood sugars. It is necessary therefore to point out here that when the regular insulin is replaced by the protamine-insulin sugar generally reappears in

the urine for a number of days. In time, however, this condition is brought under control. Such temporary glycosurias have also been noted by Joslin⁸ and Wilder.⁷

EFFECTS OF PROTAMINE-INSULIN ON THE CHOLESTEROL CONTENT OF BLOOD PLASMA

Aside from the experiences with blood and urinary sugar and the clinical conditions in general, better control of the diabetes in the "insulin-waster" is also suggested from experiences with plasma cholesterol. To date, the average plasma cholesterol of 200 determinations in our cases since treatment with protamine-

TABLE III.

SHOWING DOSAGES OF PROTAMINE-INSULIN, THEIR INCIDENCE AND CORRESPONDING NUMBER OF REACTIONS

Units	Number of Injections	Reactions
30	16	0
40	23	1
50	74	0
60	193	9
70	1	0
80	226	6
90	31	9
100	73	4
120	50	12
140	35	1

TABLE IV.

SHOWING FREQUENCY OF REACTIONS WITH DIFFERENT DOSAGES OF PROTAMINE-INSULIN ADMINISTERED TO DIABETICS WITH NORMAL BLOOD SUGARS BEFORE THE INJECTION

Units	Number of Injections	Reactions
60	3	0
80	14	1
90	9	1
100	5	0
140	1	0

insulin is 0.187 per cent; whereas, in the same cases the average of the last 200 determinations before institution of treatment with protamine-insulin was 0.203 per cent. This difference is admittedly small, and, according to the probable error of the difference, the finding is not very significant (ratio of difference to its probable error = 1.81). Significant, however, are the findings in cases in which the cholesterol contents of the bloods have been persistently above the normal, as in the "insulin-waster", or because of complications. In one case, for example

(590/30), the average of seven weekly tests since treatment with protamine-insulin was instituted was 0.204 per cent; whereas, of the last seven determinations before this treatment the average value was 0.256 per cent, and, in this case, the difference noted was significant (ratio of difference to its probable error = 3.2).

EFFECTS OF PROTAMINE-INSULIN ON LIVER FUNCTION

Disease of the liver is very common amongst diabetics, and the enlargements of this organ in this disease appear to be due to fatty infiltration.^{11, 12} With control of the diabetes, marked decrease in the size of these enlarged livers has been noted with the regular insulin treatment also. Hagedorn *et al.*,² however, report especially good results with protamine-insulin, and that this product may be more effective than regular insulin with disease of the liver is suggested from the bilirubin contents of the bloods in some of our cases. The combined data to date show that of 200 van den Bergh tests since the institution of treatment with protamine-insulin the average amount of bilirubin in the blood was 0.49 units, whereas, in the last 200 determinations before treatment, in the same cases, the average was 0.63 units. Little significance is here also to be attached to the findings because of the probable error of the difference (ratio of difference to its probable error = 1.31). As in the case of cholesterol, however, not all of these patients had excess quantities of bilirubin in the blood. In the cases with excesses there is good reason to believe that treatment with the protamine-insulin was beneficial. Thus, in Case No. 4986/34, the average of the last six tests before treatment with the protamine-insulin was 1.26 units; whereas, since treatment, the average was 0.51 units only.

INDICATIONS FOR THE REDUCTION OF DOSAGES OF PROTAMINE-INSULIN

As stated, in order to control the diabetes with injections once a day only large doses of the protamine-insulin are necessary. There is, therefore, the factor of economy to consider, and since hypoglycæmic reactions are very uncommon some other indication must be found for the reduction of dosage. The best indication is, of course, a persistently normal blood sugar. The case shown in Chart 4 is an example. In this case, it will be noted that the dosage was reduced from 80 to 40 units. In general practice, however, when the urine is persistently free of sugar it may be taken that the blood sugar is normal or nearly so, providing the diabetes is not complicated by a condition known to increase the renal threshold of glucose—chronic nephritis, arteriosclerosis, infection, etc.

The writers gratefully acknowledge the assistance of Miss Florinda M. Matheson, Nurse-in-Charge of the Metabolism Department, during this investigation.

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AN EARLY SIGN OF INFLUENZA.—E. Soza describes a sign of influenza which he first noticed in the 1918 epidemic and has observed in all subsequent epidemics and sporadic cases of the disease. On careful percussion of the middle and posterior part of the right half of the thorax a zone of dullness is constantly found; to this

Soza has given the name of "zone of dullness of the middle lobe." This zone appears at the beginning of the disease, and so constitutes an early sign of influenza. It disappears when the disease subsides, and becomes more pronounced on the occurrence of complications.—*Guatemala Med.*, February, 1936, p. 12.

CHRONIC SINUSITIS*

BY G. EDWARD TREMBLE, M.D.,

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THE apparent prevalence of sinusitis in recent years is due perhaps to more accurate methods of diagnosis rather than to an actual increase in the disease. In order to understand the pathological conditions which involve the accessory sinuses of the nose some reference to the fundamental anatomical features of this region is necessary. These air-spaces are outgrowths from the nasal cavities and are lined with the same columnar epithelium as the rest of the nose. The cancellous tissue of the bone becomes hollowed out and the names of the sinuses correspond to the bones in which they are found, namely, the maxillary antrum, the frontal sinus, the ethmoidal labyrinth, and the sphenoidal sinus.

ANATOMY

At birth the antrum is present, about the size of a small pea, while the sphenoid can just occasionally be recognized. The ethmoidal labyrinth is the only one to be well developed at this age, and is usually the group of cells to cause trouble before the age of two years. The frontal sinus is an upward prolongation of one or more of the anterior ethmoidal cells and is rarely identified until the end of the first or the beginning of the second year. Although these sinuses are rudimentary at birth, they develop rapidly during childhood and adolescence, attaining their full growth in early adult life.

The sinuses are paired, and each one communicates with the corresponding nasal cavity by a small opening or "ostium" on the lateral nasal wall. For convenience, these cavities are divided into an anterior and posterior group, depending on the site of drainage. The antrum, frontal sinus, and anterior ethmoid cells open close together in the middle meatus or groove below the middle turbinate. (The anterior ethmoidal cells are two to eight in number.) They compose the anterior group of sinuses. The posterior group is formed by the posterior ethmoidal cells and the sphenoidal sinus, com-

municating with the superior meatus and with the spheno-ethmoidal recess immediately above and behind the superior turbinate. (The posterior ethmoidal cells are one to seven in number.) The attachment of the middle turbinate divides the sinuses into the anterior and posterior group. The clinical importance of this anatomical feature lies in the fact that pus

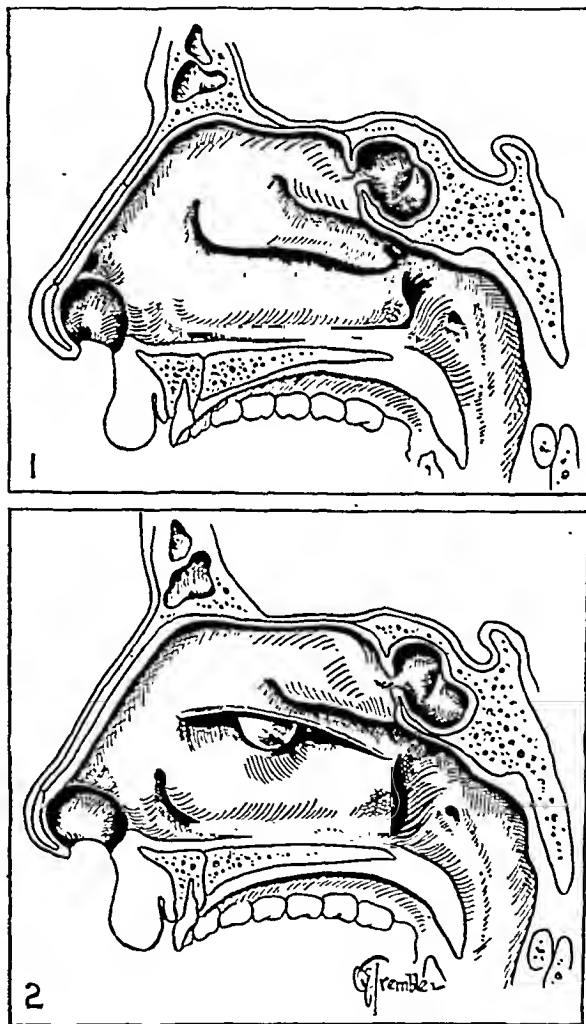


Fig. 1.—The right wall of the nasal cavity with the mucous membrane showing the three turbinates, the inferior, middle and superior. Below each turbinate is the corresponding groove or meatus into which drain the various sinuses. Behind the superior turbinate at the right is the sphenoidal sinus and below just posterior to the inferior turbinate is the opening of the Eustachian tube. Fig. 2.—Shows the right wall of the nasal cavity after removal of the middle turbinate. The nasolacrimal duct opens under the inferior turbinate anteriorly. The frontal sinus, antrum and anterior ethmoid cells (the anterior group of sinuses) open into the middle meatus, in front and behind the rounded surface or bulla, that is, below the cut edge of the middle turbinate. The posterior ethmoid cells and the sphenoid (the posterior group) drain into the groove below the superior turbinate and into the recess just above.

* Read before the McGill Reporting Society, February 10, 1936.

From the Otolaryngological Department of the Royal Victoria Hospital.

in the middle meatus, that is, below the middle turbinate, arises from the anterior group, while pus above the middle turbinate in the olfactory fissure comes from the posterior group. The problem then is to determine which cell or combination of sinuses is the source of the infection. By the process of elimination this does not appear difficult, but on account of the marked anatomical variations in this situation it is not always simple.

PHYSIOLOGY

Little is known regarding the physiology of these cells. They serve to warm, filter and moisten the inspired air. They also act as resonating chambers to modify the voice. Finally, these large air-spaces add lightness to the skull.

HISTOLOGY

The nasal mucous membrane is a thick vascular lining with large cavernous spaces in definite areas, and innervated by the second division of the trigeminal nerve, with its associated sphenopalatine ganglion. It is composed of a layer of fairly loose connective tissue, particularly over the middle turbinate, which is controlled by unstriated muscle fibres. In addition to the erectile tissue layer, elastic fibres are present, especially adjacent to the periosteum. This forms an elastic tissue framework which causes the mucosa to swell or shrink at the slightest irritation. The mucous membrane is composed of ciliated columnar epithelium interspersed with mucous secreting "goblet cells" which open upon the surface.

The normal mucous secretion from the nose has the power of inhibiting the growth or rendering harmless, dust or organisms inhaled with the air. Owing to the cilia there is also a definite sweeping action toward each ostium and then backward into the nasopharynx. Under certain conditions, namely, lowered resistance, numerous virulent organisms, trauma, etc., the mucous membrane loses its power to warm, moisten and filter the air, and infection is likely to take place. Regarding the frequency of chronic sinusitis it has been estimated that at least 2 per cent of the population are affected.

The diagnosis of "nasal catarrh" is responsible for the overlooking of by far the larger proportion of cases of chronic suppuration in the nasal accessory sinuses. Too often the physician agrees with the patient that it is

more or less an incurable inconvenience. As a result the patient frequently suffers from headache besides the post-nasal discharge, and his general health is affected in various ways. Until recent years, the occurrence of sinusitis in young children has been overlooked because the symptoms were very like those of "adenoids", and the removal of these growths frequently cured the inflammation of these cells.

CHIEF CAUSES

The vast majority of sinus inflammations are of intranasal origin, and they arise from specific infections. Over 90 per cent of the cases fall into this group. In order of frequency, diphtheria, scarlet fever, and measles are mainly responsible for sinusitis in childhood, while influenza is the most prolific infective agent in adults. A small minority, perhaps 5 to 8 per cent, are caused by local infection, and the most prominent of this class are those cases brought about by diseased conditions of the teeth.

Inflammation may be limited to one or more of the sinuses on either or on both sides of the nasal cavities. As a result of infection from the teeth the maxillary antrum is often the only sinus affected, whereas it is unusual to find the frontal, ethmoidal or sphenoidal sinuses the sole focus of inflammation. This is due to the fact that the roots of the 2nd bicuspid and 1st molar teeth are adjacent and sometimes project into the floor of the antrum.

Age incidence.—Suppuration of the nasal accessory sinuses is generally met with after the age of puberty. Nevertheless, as mentioned above, many cases are seen in children, especially as a complication of the infectious diseases and typhoid. This should be borne in mind in cases of obscure pyrexia in children, in multiple arthritis, and in those patients where a purulent nasal discharge persists after the adenoid has been thoroughly removed.

Signs and symptoms.—Obviously, it is a difficult matter for anyone who does not devote his entire time to this type of work to detect which sinus or combination of sinuses is the source of infection. However, there are certain signs and symptoms which should lead a thoughtful physician to suspect the general situation of an infective process. Acute inflammation of the sinuses is usually manifested by severe pain, nasal discharge, superficial swelling and tender-

ness to pressure, while the chronic cases are liable to be overlooked owing to the lack of symptoms.

General symptoms.—To a certain extent there is a marked similarity in the symptoms, whether one or more of the sinuses are involved. The chief complaints of the patient are: (1) nasal discharge; (2) headache, and (3) nasal obstruction.

As a rule the discharge in chronic cases is unilateral, has a foul odour, and is mucopurulent in character. It escapes from the nostril when the antrum, frontal or anterior ethmoidal cells are affected, but into the nasopharynx and throat if the discharge issues from the posterior ethmoidal and sphenoidal sinuses.

Headache varies in situation and degree according to the cells involved and the many circumstances which may hinder free drainage of the purulent material. Intense pain in the upper jaw or teeth of the affected side is characteristic of acute maxillary sinusitis, whereas, in chronic suppuration frontal headache most often indicates disease of one or more of the anterior group of sinuses, that is, the antrum, frontal sinus or anterior ethmoidal cells. Pain referred to the eye or the root of the nose would suggest involvement of the ethmoidal region. Occipital ache, pain over the vertex or the temporal region, would make one suspect infection of the posterior group of sinuses, namely, the posterior ethmoidal cells or the sphenoidal sinus. In typical cases, the headache is intermittent and depends on the drainage.

Frontal headache in the morning, diminishing in intensity towards the early afternoon, usually indicates frontal or ethmoid involvement. The discharge accumulates in the sinuses at night while the patient is recumbent. Then in the morning, when the upright position is assumed and the dependent position of the ostia facilitates drainage, the headache usually wears away. Supra-orbital headache increasing in intensity towards the afternoon generally means infection in the antrum. This sinus drains better in the recumbent position. In the walking upright position, the ostium being high above the level of the floor of the sinus, drainage is retarded. The opening, in fact, is near the roof of the antrum, just below the orbit, so that the antrum has to be almost full of pus in the erect position before the overflow appears in the nose.

Occipital headache in the morning, becoming

intensified toward the afternoon, often indicates sphenoiditis, because the ostium of the sphenoid, like that of the antrum, is above the level of the floor of the sinus and therefore poorly placed for drainage in the upright position.

Nasal obstruction.—This is present in acute sinusitis and in most of the chronic cases. It is caused by inflammation and œdema of the nasal mucosa, which varies with the amount of discharge that accumulates in the nose. The obstruction is intermittent and alternates from side to side, but usually the diseased side is more markedly affected.

An additional and frequent factor in the production of nasal blockage in chronic suppurative is the presence of nasal polypi. These curious structures when examined microscopically reveal the histological essentials of chronic inflammation of the mucous membrane from which they grow. In appearance a polyp resembles a skinned grape and should not be confused with any other condition. As a rule it is white or bluish-white in colour, and is gelatinous in consistency. Whether single or multiple, nasal polypi most frequently arise in the ethmoidal cells, and are indicative of inflammation of the underlying periosteum and bone.

BACTERIOLOGY OF THE SINUSES

Bacteria are always present in the nasal mucous membrane, but are kept in abeyance by the normal defences of the body. The organisms which are usually found in sinusitis are seldom in pure culture. The commonest ones are the pneumococci, types II, III, and IV, *S. hemolyticus* and *non-hemolyticus*, *Staphylococcus*, and *B. influenza*. These cultures are obtained from the discharge as it comes from the nose or the washings from the individual sinuses on suitable culture media. When the body resistance is lowered by debility or disease, or the nasal mucosa is affected by trauma, the bacteria are able to penetrate and invade the sinuses. The incubation period varies according to the infecting organism, but it is generally within two or three days. Infection usually begins with an acute rhinitis, but instead of subsiding in a few days it progresses and localizes in one or more of the sinuses.

Without going into detail as to the usual methods of diagnosing a diseased sinus, let us consider some of the remote manifestations of chronic sinusitis.

SINUSITIS AS A FOCUS OF INFECTION

In addition to the three cardinal symptoms of discharge, headache and nasal obstruction there are many others, which vary in nature, degree and situation according to the severity of the infection and the region involved in the inflammatory process. As a general rule, serious complications, whether of a local or remote character, are more likely to follow an acute exacerbation of a chronic infection than as a sequence of a primary acute inflammation. When such foci exist in the frontal, ethmoid and sphenoidal sinuses, there is always the danger of extension into the orbit. Even more serious are the possibilities of such intracranial complications as cavernous sinus thrombosis, cerebral abscess and meningitis.

Direct infection of the lower respiratory and the upper gastro-intestinal tract also takes place when infective material drops down from the nasopharynx into the trachea or œsophagus. Secondary infection from the sinuses through the blood stream may occur anywhere in the body, but the more common sites are the smaller joints and tendons, giving rise to the so-called "rheumatic symptoms". The endocardium, myocardium, pericardium, the bronchi and kidneys, are also similarly affected. Naturally, the symptoms vary according to the site of the lesion, but in childhood significant signs are headache, anæmia, cough, pulmonary affections, low-grade fever and particularly multiple arthritis. It is true that similar results may be caused by infection from tonsils and adenoids, and, consequently, when these structures have been thoroughly removed the occurrence or the continuation of the above symptoms should make one suspect the sinuses.

The evidences of toxic absorption from these regions are more common in children than in adults, because the bony walls of the sinuses and the cancellous tissue which surrounds them is softer and more vascular. In addition to this there is not the same degree of immunization in a child as in one of more mature years. Concerning the remote manifestations of sinus disease in adults it should be mentioned that gastric, pulmonary and ocular symptoms are more frequent than cardiac, muscular or arthritic complications. The constant swallowing or inhalation of septic matter are probably responsible for the first two. One of the most striking results of the removal of a septic focus in the

nose is improvement in the appetite and general health which follows relief from symptoms of stomach disorder.

The pulmonary affections referred to are chronic bronchial catarrh, bronchitis, and, not infrequently, asthma. In consulting his physician for these complaints the patient often makes no mention of a previous "chronic nasal catarrh" which only caused an inconvenience, because to him the pulmonary trouble is the real grievance. Now the great majority of chronic nasal catarrhs are really muco-purulent discharges from the nasal sinuses, and the infective micro-organisms which cause them will often be found in the patient's sputum. Still more important is the fact that if the source of infection is removed its complications in the lower air-passages will often disappear without any further treatment. In other words, "chronic nasal catarrh" is more often a symptom than a disease by itself, and its causation is infection in one or more of the nasal accessory sinuses.

DIAGNOSIS

The sinuses as a focus of infection are frequently overlooked because they may be the cause of a latent infection with little or no purulent discharge and few definite symptoms. The history is very important, particularly if the patient complains of repeated colds in the nose, suppurative sinusitis, or acute lymphadenitis. Lack of aeration or interference with drainage from the sinuses, as evidenced by a deflected septum, septal spurs, or hypertrophied turbinates, should receive thoughtful consideration. The recognition of acute sinusitis as a rule is quite simple, but that of chronic inflammation with little or no discharge is often a difficult matter.

Once the diagnosis is made there is only one cure, namely, to open the cavity freely, remove the diseased membrane, and establish free drainage into the nasal cavity. In chronic infection, there is only a moderate increase in the leucocyte count, usually from nine to twelve thousand, with a slight destruction in the number of red cells. It follows, therefore, that in all cases where an inflamed accessory nasal sinus is under suspicion, especially from the point of view of systemic symptoms, we should submit its contents to a skilled bacteriologist who would inform us as to the nature and virulence of the secretion.

STUDIES IN MINERAL METABOLISM*

I. CALCIUM AND THE KIDNEYS: CLINICAL

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RENAL rickets is a disease of infancy, childhood or adolescence in which rickets, like lesions of the bones, is associated with chronic nephritis. The name "renal rickets" implies that the nephritis in some way causes the bone lesions. In a previous paper¹ I have questioned this and suggested that the reverse may be true, that a hyperealeæmia due to the bone disease causes the nephritis. In the present paper an attempt is made to show just what does happen in man when calcium assaults the kidneys for varying lengths of time. Suggestions are also made associating the end-results with renal rickets and with pyelonephritis. The picture is admittedly very incomplete, but it is hoped that this communication may serve as an outline into which the details may be filled.

1. *The first calcium lesions in the kidney.*—A number of instances of renal calcification in infants, due apparently to the toxic effects of ergosterol which had been irradiated in a faulty way, have been reported in German journals. (*Vide* ref. 2 and 3 for bibliography). Unfortunately these reports are not available to me. Thatcher⁴ recorded the history of an 18-months old child with calcium deposits in the kidneys, which he thought were due to vitamin D. I think it not certain that this was the causative factor. *Post mortem* the cortex of the kidney was free, whereas calcium deposits were scattered through the medulla, chiefly in the collecting tubules. Although it was thought that these were simple intratubular precipitates there was cellular fibrous tissue about some of the containing tubules. Some tubules were dilated and contained pus, which was interpreted as indicating the presence of infection. There was stated to be no evidence of rickets past or present, but a microscopic description of bone was not recorded.

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Reginald Lightwood⁵ recently reported finding insoluble calcium salts in the renal tubules of six infants who had had poor appetite, were constipated, wasted and hypotonic. Sometimes their urine had contained a little albumin, a few leucocytes, and bacilli. The pyuria failed to respond to the usual treatment. There was no evidence of parathyroid or other endocrine disturbance, the feeding could not be blamed, and vitamin D preparations had not been given in excess. The immediate cause of death was a terminal infection.

I have seen three babies who had calcium deposits in their kidneys.

CASE 1

Terence C. (No. 34-6771), aged 4½ months, was admitted to hospital in January, 1934, because of loss of weight. Weighing 8½ lbs. at birth he gained rapidly for six weeks, then developed colic and lost weight slowly. Supplements to breast feeding did not improve his condition. He became constipated, developed an abscess on the cheek and one on the breast, and then nasal catarrh. For a week prior to admission he was given 10 drops of viosterol (irradiated ergosterol in oil) daily. On admission he was not very ill, but he was restless and cried out as if in pain; temperature 101° F.; weight 9 lbs., 12 oz.; marked craniotabes; both kidneys palpable, hard and nodular. The urine, passed in a good stream, repeatedly contained cells; *B. coli* and staphylococci were grown from it. Blood calcium, 12.5 mg.; blood urea, 40 mg.; white blood cells, 18,000; polymorphonuclears, 40 per cent. Intravenous pyelography was attempted but the infant collapsed. Two days later his temperature rose to 107° F. and he died.

The pertinent findings at post-mortem were, (1) broncho-pneumonia, (2) marked craniotabes, (3) costochondral junctions barely palpable after removal of skin and muscle, (4) tibia grossly normal, (5) a small thymus, (6) right kidney came to 1 cm., below pelvic brim, left to brim; both were enlarged, lobulated, hard; the cut surface pale, with yellowish gritty flecks running in the direction of the tubules toward the base of the pyramids; pelves, ureters, bladder and urethra were normal.

Microscopically, in the kidney there was an almost normal cortex, a few tubules being slightly dilated, lined by flattened epithelium, and filled with a homogeneous pink staining material. Large roundish cells lay on the surface of this material in some cases. In sudden contrast, the medulla was heavily splashed with calcium (Fig. 1). Together with some pink material and a few round cells some of the calcium lay in the lumina of tubules, but the bulk of it was in round or oval masses just outside the tubular epithelium. These masses apparently filled vessels, and since blood could not be seen in them and could be seen in neighbouring capillaries I

interpreted the containing vessels as lymphatics (Fig. 2). They bulged the walls of the tubules in, the latter being distorted by pressure and by dilatation. There was no calcium in the epithelial cells. No pus was seen. The pelves and ureters were normal. No calcium deposits were found in the other organs. At the costo-chondral junction there was no zone of hypertrophic cartilage cells, no increase in osteoid tissue; the trabeculae abutting upon the cartilage were short and twisted. There were no osteoclasts, no signs of inflammation, no hemorrhages. The cellular marrow reached to the cartilage. The picture was one of cessation of growth and of local atrophy, but it offered no suggestion as to the cause.

CASES 2 AND 3

Gwen L. (No. 32-3379) and Jean L. (No. 34-8391) have already been reported, but from a different angle.¹ They were sisters, born two years apart. Both had severe congenital rickets. Both became dwarfs. Both had a high blood calcium level, 14.9 to 19.0 mg., with a normal or slightly lowered inorganic phosphorus level, 4.8 to 3.0 mg. Both had calcium deposits in the kidneys. Neither had enlarged or diseased parathyroid glands. The second had a malformed pituitary; the first may have had. It was suggested that they were early examples of one form of so-called renal rickets, and that at least in some cases the sequence of events in this

disease is pituitary malfunction, faulty bone metabolism, hypercalcemia, renal injury, and renal destruction.

The first baby, Gwen L., who died at three months, had kidney lesions like those of Terence C., above, with added deposits in the cortex and a few pus cells in some tubules. In the kidneys of Jean L., who died at six months, there were many lesions in the cortex (Fig. 3) but more in the medulla. They were still almost entirely interstitial, prominently peritubular. Not only were the tubular walls carried in by intruding masses of calcium but also by granulations due to calcium irritation (Fig. 4). This led to a curious appearance as of one tubule holding in its lumen another smaller one, which in turn was filled with loose granulation tissue or with calcium. In some places the wall of the tubule had broken down, the dilated tubule containing pus (Fig. 5). In the cortex there were what appeared to be distended lymphatics. Small areas of interstitial lymphocytic infiltration were to be seen. There was as yet practically no fibrosis. The glomeruli and blood vessels did not appear diseased.

We may say that when calcium deposits occur in the kidneys of young infants they may, in some cases, apparently be entirely intratubular (Lightwood) or almost so (Thatcher



Fig. 1.—Kidney of Terence C. (X 20). Contrast the clean cortex with the calcium bespattered medulla. All the tissues illustrated in this article were fixed in formalin, blocked in paraffin, stained with silver nitrate, hematoxylin and eosin. Fig. 2.—Collecting tubule of Terence C. (X 400). The mucosa of the dilated tubule has been artificially drawn away from the stroma bringing into sharp definition the positions of the two calcium masses (A) in the wall of the tubule. It is suggested that these masses lie in distended lymphatics. Similar masses at (B). Loose calcium at (C). Fig. 3.—Cortex of Jean L. (X 150). There is intra- and extra-tubular calcium; distortion of tubules by pressure. Some tubules contain pus, and others are filled with albuminous material. Fig. 4.—Tubule in medulla of Jean L. (X 400). A granulation, the result of such calcium injury as is shown in Fig. 2, extends into an enormously hypertrophied tubule. Compare the size of the normal nearby tubules. Fig. 5.—Tubule in the medulla of Jean L. (X 300). The distorted tubule contains pus. Recognizable calcium (jet black) forms but a small part of the collar of amorphous material surrounding the tubule. The bulk of the injury may perhaps be due to calcium in solution.

and McGregor) and yet cause inflammation in the kidney, with albumin, pus and bacteria in the urine. In other cases the deposits are chiefly interstitial, causing lymphatic obstruction, tubular distortion, necrosis, and dilatation and focal inflammation. Again albumin, pus and bacteria are found in the urine.

2. *Second stage.*—By the friendly cooperation of Drs. Gilbert Adamson, William Boyd and A. T. Cameron⁶ I am able to quote an instance of more severe mineral damage to the kidney, due, in this case, to destruction of bone by metastatic bronchogenic carcinoma.

CASE 4

A man of 18 (No. 10274) was admitted to the Winnipeg General Hospital in March, 1934, and died there four months later. The skeleton was probably widely involved for six months before death. He had had no urinary symptoms until a week before admission, when frequency set in. His urine at times contained a little albumin, a few granular casts, red cells and pus cells. His blood calcium ranged between 15.0 and 19.0 mg., and his inorganic phosphorus between 3.6 and 5.7 mg. At autopsy there was slight surface involvement of the kidneys by tumour tissue. The cut surface was pale with some loss of markings, and with yellowish streaks running through the cortex and medulla. Microscopically, there was calcium in the interstitial tissue of the cortex and medulla and in the lumina of the tubules, but none in the glomeruli. There was moderate, patchy fibrous replacement of tubules. On the other hand some tubules were dilated even to twice the diameter of a glomerulus, and were filled with a pink or greyish blue staining material. Here then the calcium injury has produced atrophy, fibrosis, and dilatation.

3. *Late lesions.*—The heaviest, long continued, excessive excretion of calcium and phosphates takes place in chronic hyperparathyroidism. Fuller Albright and his associates have repeatedly emphasized the renal lesion in this disease. In two studies,^{7,8} they listed from the literature the post-mortem finding in 22 cases. Contracted kidneys were found in at least 16, calcium also being present in epithelium, tubules or interstitial tissue in 16. This apparently was the only mark distinguishing these kidneys from simple chronic interstitial nephritis. Pelvic stone is present in about 25 per cent of all cases of hyperparathyroidism.

In multiple myeloma destruction of the kidney may also take place, but the picture is complicated by the injury due to Bence-Jones protein.

CONCLUSIONS AND SUGGESTIONS

Calcium injury of the kidney begins with the laying-down of intratubular and peritubular calcium, and passes by way of obstruction, dilatation and collapse of tubules, and by way of

interstitial fibrosis to complete destruction. What is left is a sclerotic fragment with or without calcification of the substance, or stone in the pelvis. The fact that calcium may be absent at the last is important.

In renal rickets, too, the kidney at time of death is but a sclerotic fragment, usually extremely small, oftentimes with dilated pelvis, sometimes cystic. It does not so much resemble the kidney of hyperparathyroidism as that of chronic pyelonephritis. Indeed, it is probably indistinguishable from the latter, for, in the studies of this disease by A. G. Gibson⁹ and by Warfield Longcope and W. L. Winkenwerder,¹⁰ 3 of their 20 patients probably had renal rickets. On the other hand, pyelonephritis is not clearly separable from hyperparathyroid nephritis, for Longcope and Winkenwerder's case 6 with the former disease is the same patient as Albright's⁷ case 16 with the latter. There is a fading of one picture into another. This, I suggest, indicates the action of one major, common, causative factor, with minor, variable factors. I believe that the major factor is calcium, and that the variables may be the height of the calcemia, its duration, the time of its occurrence, the source, and hence the physio-chemical state, of the calcium, or the presence or absence of associated hyperphosphaturia or superadded infection. Two last facts strengthen the suggestion that calcium is the major factor. First, not less than 8 of the 20 cases of chronic pyelonephritis gave evidence suggesting upset mineral metabolism, *i.e.*, high blood calcium, or bone disease, or renal stone. Second, in at least 7 cases of renal rickets increased blood calcium has been found.^{11 to 17} These facts must be looked upon as of major importance and no longer as incidental, now that we are beginning to realize what high calcium excretion may do to the kidney.

The microphotographs illustrating this article were kindly taken by Miss Nason, of the University Department of Pathology, by permission of Prof. William Boyd.

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EXPERIENCES IN LEG LENGTHENING*

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THE subject of leg lengthening is of vital importance to those patients who are unfortunate enough to have a short extremity. They must wear an unsightly and heavy lift of some sort, or they must be content to walk with an awkward gait, and bear with what fortitude they have the compensatory deformities which inevitably develop. If a lift is not worn to equalize the length of the legs, the pelvis is constantly tilted, and a scoliosis develops which may seriously handicap the patient. A lift, as well as being unsightly, means extra weight on an already weakened extremity. What doctor has not had patients ask if anything can be done to correct shortening of an extremity? What doctor has not felt at least a little guilty because of the patients' disappointment if the answer be in the negative?

It is necessary and just that all those interested in orthopaedic surgery make themselves familiar with the best methods of correcting inequality in the length of legs, and be prepared to offer their patients the benefits thereof. Codivilla¹ and Putti² showed that lengthening was a practical procedure, that it must be done gradually, and that skeletal traction and counter-traction should be used. They proved that it was the fascial structures of an extremity that provided the greatest resistance to lengthening, and that blood vessels and nerves would tolerate considerable gradual extension. It remained for Abbott³ to devise an apparatus and a surgical technique that was practical. He should get full

credit for giving this work the necessary stimulus on this continent.

Abbott described a form of osteotomy which left considerable bone surface in contact when lengthening was complete, and he devised an apparatus to maintain accurate alignment as well as extension. Various modifications of his technique and apparatus have been reported, but the fundamentals are not changed and might be listed as follows: (1) skeletal traction and counter-traction; (2) slow and gradual lengthening; (3) a form of osteotomy which leaves considerable bone surface in contact when lengthening has been completed; (4) wide division of the fascia; (5) some form of stabilizer to maintain accurate alignment of fragments; (6) rigid surgical technique; (7) postponing of stabilizing operations until lengthening has been completed.

The purpose of this presentation is to stimulate interest in the subject, and to report a few cases upon which leg lengthening has been performed. The cases chosen illustrate shortening due to various causes and several difficulties which may be encountered. From these experiences one may form an opinion as to what types of cases are suitable for leg lengthening, and also what might be considered the ideal case for this procedure. Details of technique and apparatus will not be described, because time does not permit. A modified Abbott machine was used in all cases.

CASE 1

D.K., aged 15. Infantile paralysis at eighteen months of age, followed by extensive paralysis of left leg, including the quadriceps. Walked with the aid of crutches and a long leg brace until fourteen years of age. November, 1928.—Triple arthrodesis, fixation of tendo Achillis, and transplantation of the semimembranosus tendon to the patella.

* Read at the Combined Annual Meeting of the American and Canadian Medical Associations, Section on Orthopaedic Surgery, June 13, 1935.



Fig. 1

Fig. 2

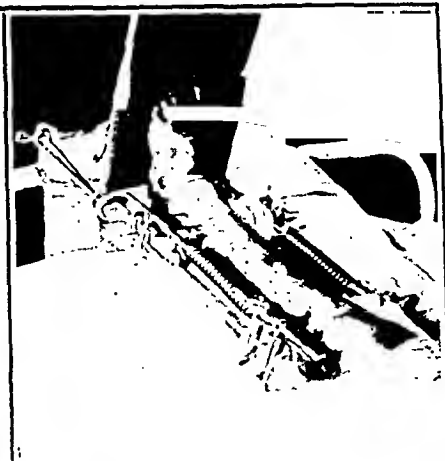


Fig. 3

Fig. 1 (Case 1).—X-ray after lengthening was complete but with the apparatus still in position. Fig. 2 (Case 1).—Five and one-half years after operation, showing very little evidence that any operation has been performed on the tibia. Fig. 3 (Case 1).—Apparatus in position.



Fig. 4 (Case 4).—Condition: A, in April, 1930; B, in May, 1935. Fig. 5 (Case 4).—Shortening in January, 1930. Fig. 6 (Case 4).—Appearance in May, 1935, with the cumbersome apparatus worn before lengthening and the shoe worn at present. Fig. 7 (Case 5).—Condition in March, 1933, showing a weak bridge of bone supporting the leg, and in November, 1933, showing the fracture and the bone graft in place. Fig. 8 (Case 5).—Well healed and strong tibia in May, 1935. Fig. 9 (Case 5).—Appearance before and after the lengthening.

May, 1929.—Lengthening of left tibia (2¾ inches obtained). The leg was supported in a plaster cast for six months. The patient now walks well without any appliance and the legs are equal in length.

CASE 2

K.D., aged 15. Atrophy of the right leg due to infantile paralysis. Two inches of shortening.

July, 1932.—Lengthening of the right tibia (2½ inches obtained). The leg was supported in a plaster cast for six months. Moderate infection developed, but cleared up without trouble. At present the girl walks well. Her legs are equal in length.

CASE 3

J.L., aged 21. The right leg 1½ inches short, due to mal-union of a fracture of the right femur five years before.

October, 1932.—Lengthening of right tibia (1½ inches obtained). The leg was supported in a plaster cast for about seven months, but the patient was able to return to work in four months. Moderate infection developed, necessitating the curetting of a sinus from the tibia in December, 1933, after which the infection cleared rapidly.

CASE 4

E.W., aged 18. This girl had most of the soft tissues of the left leg torn away by an accident at four years of age. When ten years old the left knee was resected, to correct a flexion deformity of the knee, and both epiphyseal lines were removed. When I first saw her in 1930 she had a bony ankylosis of the left knee in about 20° flexion. A thin scar surrounded the leg from the knee to four inches above the ankle. She was wearing a lift, 8½ inches high, under the left foot.

January, 1930.—An Hefferich's osteotomy was performed to allow straightening of the knee without losing any length.

March, 1930.—Lengthening of left femur (3 inches was obtained). Altogether, after operation her left foot was 5½ inches closer to the floor—3 inches by lengthening the femur and 2½ inches by osteotomy of knee, and she now requires a 2 inch lift built into her shoe to walk comfortably. She was unfortunate enough to fracture her left femur one and a half years after the lengthening through the same area in which the lengthening was done, but union took place in the usual length of time. There was mild infection about the lower end of the upper fragment after lengthening.

CASE 5

W.K., aged 17. Left leg 4 inches short, due to healed tuberculous arthritis of left hip joint.

October, 1932.—Lengthening of left tibia (2 inches obtained). Bony union in the upper part of the tibia was delayed, and about six months after operation a fracture occurred through this area. Healing still did not take place, so a bone graft was placed across the fracture in September, 1933. Healing then progressed rapidly. At present he walks quite well, with about 1½ inch lift inside the left shoe.

The average lengthening obtained was approximately 2¼ inches. Troublesome infection occurred in three cases, but no serious osteomyelitis developed. Although fairly satisfactory results were obtained even in these cases, one feels that more lengthening might have been obtained if infection had not been present. This was particularly true of Cases 4 and 5. Safe bony union was slow in all patients. It was

necessary to keep the leg supported for at least six months, and about eighteen months in Case 5, where a bone graft was required. There was some trouble because of tilting of the fragments during lengthening in two cases, and the apparatus is now provided with a stabilizer to correct this defect.

The results are gratifying to the patients in spite of the discomforts and dangers, and all of them feel that the time was well spent. The entire period is not necessarily wasted because further rehabilitation is possible during convalescence. Two of these patients took courses in shorthand and stenography during their treatment, and have subsequently found remunerative positions.

In these cases the operation was performed where shortening was due to: (1) infantile paralysis; (2) healed tuberculosis of the hip joint; (3) mal-union of fracture; (4) growth disturbance due to destruction of epiphyseal lines.

One hesitates to be dogmatic about the amount of shortening necessary to justify operation, but the author feels that it should never be done for less than 1½ inches. Each case, of course, should be individualized, and the psychological effect of a short extremity and an unsightly lift on both the patient and a prospective employer must never be forgotten.

If the shortening is due to infantile paralysis, and the patient is able to walk without a brace (perhaps after various stabilizing operations) leg lengthening should be done. But if the quadriceps is paralyzed and cannot be replaced, a long leg brace is usually necessary, and lengthening would appear to be too formidable a procedure for the benefit obtained. The ideal type of case, of course, would be one in which the extremity is normal except for its length. This condition is most closely approximated where shortening is due to mal-union of a fracture or to healed tuberculous arthritis of a hip joint. Apparently the blood vessels and nerves will allow the extension necessary, provided they are stretched very slowly. If lengthening is too rapid the foot may show temporarily a little coldness and numbness.

The operation must not be undertaken lightly. It should be done only in a hospital where rigid surgical technique and adequate after-care can be obtained. The surgeon should have some mechanical inclination and sufficient training in major bone surgery.

Patients who undergo the operation should be prepared to give up about six months. The ideal time in the patient's life is at 15 or 16 years of age, when growth is nearly complete, but before the wage-earning period. There is no reason, however, why the operation cannot be performed at practically any age. The entire process is a formidable one, but, judging from my own experience and the reported experience of others, it is quite a justifiable procedure, and should be

added to the armamentarium of all those who undertake the surgery of eripples.

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URETEROPELVIC (RENAL) OBSTRUCTION IN THE YOUNG*

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RENAL obstruction at the uretero-pelvic junction occurs in childhood more often than is fully recognized. It is usually discovered in adult life when the condition, having been prevalent for years, has done considerable damage to the organ involved and often results in the loss of a kidney. It is from the conservative point of view that this particular subject appeals to me, because if these lesions were revealed in the earlier years the function of many of these kidneys could be sustained, improved, and returned to normal by conservative renal surgery. These conditions pass unrecognized because usually until infection is added to the picture the urine is normal. The block at the obstructing point is of varying degree and probably never becomes complete, except for temporary periods, until complications arise, such as infection, stone formation, and other factors brought on by the passing of time. When these are present it is often impossible to be conservative in the treatment of the existing condition.

I wish to express the importance of early recognition, and I think a careful history will bring out recurrent periods of pain (various degrees) referable to the organ involved. Physical examination often discloses some degree of palpable kidney. Plain skiagrams, except for showing the presence of calculi or a very much enlarged kidney outline, are negative. Pyclograms will reveal, without doubt, the presence of obstruction, and functional

pyelograms, such as obtained by the intravenous route, will show the obstruction, plus the ability of the kidney pelvis to empty. Since hydronephrosis is caused by mechanical obstruction to the outflow of urine from the pelvis of the kidney, ureteral blockage—at the area of uretero-pelvic junction—from any cause will produce it. The more frequent causes of this obstruction are the following.

1. *Aberrant, accessory or anomalous vessels.*—It is well known that anomalies of the blood supply to the kidney are common and various. Though normally a single renal artery enters the renal hilus this may be doubled, due to early branching, or there may be a double artery throughout the whole extent from aorta to kidney. Of more interest are those cases in which the vascular supply does not enter the kidney at the hilus but at either one or both poles. There may or may not be a vessel occupying the normal hilus position under these circumstances. When there is a polar vascular supply the artery going to the lower pole is frequently found in close relation to that portion of the renal pelvis which is nearest to the ureter. Here the artery may maintain its normal position anterior to the pelvis, or it may run posteriorly, or, again, in some instances in which there are two vessels entering the lower pole of the kidney they may run on each side of the pelvis. The central origin of such anomalous vessels has been found to be variously from the aorta itself as an independent branch, or even from the spermatic, ovarian or iliac arteries. It will be, of course,

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readily recognized that such anomalous vascular distribution to the kidney is a persistence in part of the earlier fetal condition normally present in the mesonephros, and that with the final ascent of the kidney to its position in the renal fossa some of the blood vessels which are normally absorbed have failed to become so.

2. *Abnormalities in position.*—(a) *Abnormal rotation* of an otherwise normally developed kidney may occur in two ways: (1) by failure of or cessation of rotation (incomplete); and (2) by excessive reverse rotation. Anomalous rotation with fusion, ectopy or other malformation is frequent, but anomalous rotation alone may cause obstruction. The pyelogram may show little evidence of pyelectasis, or it may show a minor or moderate degree with clubbing of the calyces. Aberrant blood vessels are found at operation, binding the kidney in its abnormal position. Freeing the kidney has relieved many patients, with sometimes necessary plastic operations and nephropexy.

(b) *Abnormal position.*—Displacements may be unilateral, bilateral or crossed. In unilateral, the displaced kidney may lie at any point below its normal niche, but mild degrees are to be differentiated from renal ptosis (acquired) and movable kidney. Fixity in the false position is the one characteristic of congenital ectopy.

3. *High or oblique entrance of the ureter into the kidney pelvis.*—The ureter normally leaves the kidney pelvis at its most dependent portion, and in this way gravity assists in the downhill drainage. If, however, the ureter passes out from the mid portion or the upper half of the kidney pelvis the drainage from the dependent calyces is naturally uphill. Under the circumstances the musculature of the kidney works under the same strain as the bladder does when the vesical neck is pushed upward, and an analogous condition is produced. In those kidneys in which the ureter enters from the mid portion or higher up on the kidney pelvis the residual urine of the kidney pelvis slowly and gradually increases. With this increase in weight there is a tendency to descent of the kidney. Therefore with the descent of the kidney there is a corresponding ascent of the uretero-pelvic junction; thus more mechanical obstruction to the outflow of urine is produced. This ascent of the renal pelvis accounts for the ureters which at operation are seen to emerge

from the uppermost point of the hydro-nephrotic pelvis.

4. *Congenital hypertrophy of the circular layer of smooth muscle at the ureteropelvic junction.*—The normal ureteral wall consists of an outer layer, a central thick muscular coat, and the mucous membrane lining the canal. The muscular coat is composed, in turn, of smooth muscle, and is divided into three layers. The outer and innermost layers have their smooth muscular fibres running parallel to the course of the ureter. The middle muscle fibres are circular in their arrangement and their fibres pass around the ureter instead of up and down its wall. There are three points in the ureter where the middle circular layer of fibres reaches its greatest thickness. The first of these is the uretero-pelvic junction, the point where the ureter crosses the large vessels of the pelvis and the uretero-vesical junction. If in the formation of the embryo, the middle circular layer becomes abnormally hypertrophied, we have a condition of the uretero-pelvic junction that is quite analogous to congenital hypertrophic pyloric stenosis, which frequently is met with in the newborn.

The following case illustrates an example of uretero-pelvic obstruction due to some of the above-named causes.

CASE REPORT

M.F., a schoolboy, aged 9 years. There had been no previous operations and his personal and family history were essentially negative.

Present complaint.—Pain in the left lumbar area.

Onset and course.—About 2½ years before he had had a sudden onset of pain (at the time he was wrestling with his brother on the floor), in the left lumbar area. It did not radiate and was associated with vomiting. A doctor was called who gave morphia by hypodermic three times in 24 hours in order to relieve him. He also had irrigation of the bowel, as the pain was considered at this time to be due to some gastro-intestinal disturbance.

Nine months later he had a second attack of similar pain, sudden in onset with vomiting. Heat was applied to the lumbar area, which gave him some relief, but the pain gradually increased in severity and he required morphia. Ever since he had had numerous recurrences of the pain, which of late appeared to commence over the sternum, but soon became localized to the left lumbar area. More recently the pain was relieved at times by nembutal capsules, but one attack required four capsules (each gr. 1½) and then morphia. During the past three months the attacks of pain became so frequent that he had to miss considerable schooling, as each attack required some type of sedative to relieve him, and after the attack had passed he did not feel well for a few days following. After his second attack (at the first onset of sickness) he had had a flat x-ray taken, which was reported negative. The pain had never been associated with any disturbances of urination.

Examination.—The patient was a well developed and well nourished boy, appearing of the stated age. He did not appear ill in any way. For the sake of

brevity, systems showing no abnormalities are not given.

Abdomen.—There was an abdominal protuberance in epigastric area—small, soft, not tender—appearing as ensiform cartilage. The right renal area appeared to be negative. In the left hypochondriac area there was a palpable mass, more to the median line than laterally, but which could be clearly discerned with bimanual palpation to involve the left renal area also. It was firm and somewhat tender on deep pressure, not movable. The abdomen was negative otherwise.

Urine.—Completely negative. Several specimens examined in the course of one week were also negative.

Intravenous urography.—Fifteen c.c. of diodrast were injected intravenously and urograms taken.



Fig. 1.—This shows a persistent hydronephrosis on the left side, with obstruction at uretero-pelvic junction, and a normally functioning right renal tract. The illustration was taken 40 minutes following injection. The exposure at 90 minutes after injection still showed a hydronephrotic pelvis on the left, but no dye whatever on the right side.

NICOTINE POISONING.—S. Guenkin, D. Pissareff, B. Serebryanik, and S. Brown examined forty-one male and fourteen female factory hands engaged in the extraction of nicotine from tobacco leaves and in the preparation of nicotine sulphate and found that the pathological manifestations of short repeated small doses of nicotine were mainly due to disorders of the autonomous nervous system. Many of the symptoms were traceable to stimulation of the vagus; to these belong the slow and often irregular pulse, gastric hyperacidity, spasms of the non-striated muscles, salivation, and sweating. Other symptoms, such as vascular spasms in the limbs and tremors, were caused by stimulation of the sympathetic system. Some of the central nervous symptoms could be ex-

The following is the x-ray report of Dr. R. M. Tait. "Films of the kidney, ureteral and bladder regions, following the intravenous administration of diodrast by Dr. Earle Hall, show the kidneys to be normal in size, shape and position. There is a hydronephrosis of the left kidney, due to a partial obstruction at the junction of the left ureter with the infundibulum of the pelvis of the kidney, which is probably caused by a congenital stricture or a kink, possibly over a branch of the renal artery, or by pressure or traction from bands or adhesions. There is marked delay in the emptying time of the pelvis of the kidney, as it was still distended with concentrated dye after ninety minutes. No other evidence of kidney, ureteral or bladder pathology is observed."

Under general anaesthesia a left lumbar lateral incision was carried through the skin and underlying tissues and perirenal fascia opened, exposing the left kidney. The renal pelvis was isolated and found to be hydronephrotic. Visible peristaltic waves could be clearly observed passing down the pelvis and suddenly stopping at the uretero-pelvic junction, which was found to be definitely kinked and bound down with adhesions. These were removed and a small aberrant artery and vein were found to be running across the anterior surface of first portion of the ureter. These vessels were ligated and severed. The pelvis and ureter were now completely denuded of attachments, and when lying so the pelvis was observed to empty and peristaltic waves could be seen passing from the pelvis and involving the ureter. A small pyelotomy was done and a ureteral catheter inserted and passed down left ureter without meeting obstruction, there being no internal stricture or valve formation. The kidney was somewhat movable and was replaced to a slightly higher position, being held by fixation sutures involving the fibrous capsule and lower chest wall. In this position the pelvis and ureter were straightened, assuring dependent drainage and obviating any possible kinks.

The patient made an uneventful recovery and was discharged from the hospital on the tenth day after operation.

The boy has been seen at various times since, and during this seven months' period from the time of operation he has had no attacks of pain, and has been able to return to school and carry on a usual normal life.

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plained by disorders of the autonomous nervous system, which gave rise to disturbances of the cerebral circulation. Other cerebral symptoms were caused by direct action of nicotine on the central nervous system, which resulted in disturbed sleep, weakening of the memory, and neurotic symptoms. The authors add that the treatment varies according to the type of poisoning. In acute cases in the presence of symptoms of depression of the central nervous system stimulating remedies are indicated, such as strong coffee, strong tea, caffeine, eamphor, and, if necessary, artificial respiration. Atropine is useful in cases of over-excitement. In sub-acute cases the treatment is symptomatic.—*Klinicheskaya Meditsina*, 1936, 14: 21. Abs. in *Brit. M. J.*

THE MOOSE RIVER MINE ACCIDENT*

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ON Easter Monday, April 13th, an item appeared in the daily press to the effect that a cave-in had occurred at the Moose River Gold Mine, in Nova Scotia, trapping three men, Dr. E. Robertson, Herman Magill and Alfred Seadding, all from Ontario. At that time the general impression was that all had been killed as a result of the accident.

On Wednesday, April 15th, I was asked by the legal representative of the mining company to stand by to go to Moose River fully equipped for all emergencies should my services be required. Supplies sufficient for an emergency hospital were prepared, including oxygen tanks, splints, pulmotor, complete surgical outfit, concentrated foods, such as corn syrup, ovaltine, vi-tone, malted milk, ampoules of glucose 50 per cent, and special containers with an outside diameter of $\frac{3}{4}$ inch were demanded; also all available flash-lights conforming to this diameter. I was also asked to avail myself of whatever further assistance I might possibly require. Miss Anna Brennan, R.N., and Miss Ada Graham, R.N., were asked to hold themselves in readiness. Dr. W. Donald Rankin I proposed to take with me.

Indefinite reports followed one another until midnight of Saturday, April 18th, when a telephone message was received asking me to proceed with all despatch to Moose River, as communications had been established through the diamond drill hole, and it was definitely known the three men were alive. I was told the prime necessity was supervision of the food supply for the entombed men. Dr. Rankin and I fitted ourselves as best we could into the already overloaded car, and got away about 2.30 a.m., arriving at Moose River at 6.30 on Sunday morning. We arrived at the mine amidst fog and rain, which added not a little to the charm of a most desolate spot—a tumble-down shaft house, mud more than ankle-deep, and in the foreground an acre of caved-in ground. Off to the right we

could see steam rising, and here and there little groups of men.

We made our way over rocks and fallen timber to the nearest group. All were haggard and drawn, and it became at once evident that no small portion of the task would be the care of these miners, who already had been working with little or no sleep for the past week. Then we proceeded to the diamond drill hole. I wish I could describe the feelings one had as we stood about this thin iron pipe! The whole mine was quiet, save for the chatter of one far-off air compressor, for the second load of supplies had been sent down in the drill rods about fifteen minutes before our arrival. At the end of the rod was a note telling them to rap thrice on the rods when they unloaded. There squatted one of the diamond drill crew with his "ear in his hand". There stood the head driller who, for twelve hours after the drill had broken through, had tried one thing and then another in order to attract the trapped men's attention to the drill rods. He finally succeeded with a lighted pencil flash. There we were, fascinated and dominated by an inanimate piece of 2-inch pipe, which represented the only present hope for three lives, and about which our own lives were to revolve for four long days and nights.

After an hour had elapsed with no signal the rods were pulled up. They had not been touched. One should explain, perhaps, that to send down supplies, the actual drill rod was removed and a brass plug was screwed into the end of the next section. To say that we were dismayed is an understatement. Previous communications had been limited to the simple fact that the three were alive, and a request for soda and lights from Dr. Robertson. With the first load was sent brandy in small vials, grapes, chocolate, lights, and an alkaline powder. Now we were confronted by the refusal of the entombed men to unload the rods, in the face of what seemed to us to be desperate need for

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nourishment on their part. Again we loaded coffee laced with brandy, tomato soup, malted milk, vi-tone, more flash-lights and candles. These we sent down after rapping on the pipe, and again we waited for about an hour for an answering signal. None came. The rods were withdrawn.

However, it was decided of necessity to make the entombed men tell us why they were refusing to come to the diamond drill hole, and a half-hour's shouting brought an answer. "There's too much water coming down around the end of the hole!" At this, we told them

Halifax and within an hour the drone of a plane was heard and the hose dropped about 30 yards from where we stood.

Another period of shouting on our part, but this time we waited with greater equanimity for the answering hail. We told them the hose would immediately be sent down. We told them to take up the slack and stand by for food. A wooden plug was fitted into the end of the hose, and with very considerable difficulty we got it down the hole. The casing, it may be explained, only extended down the hole for 40 feet, and the rest of the journey was through the jagged path

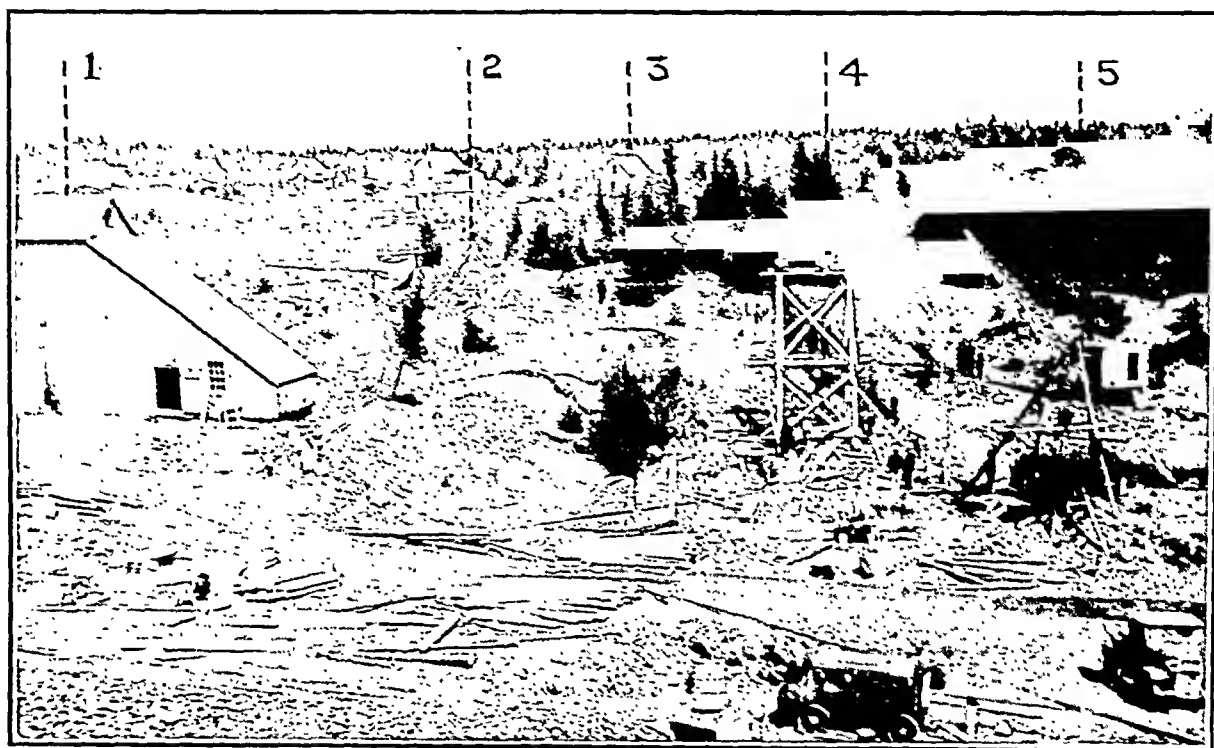


Fig. 1.—(1) Shaft house of collapsed Magill shaft. (2) Rescue shaft which became known as the Reynolds shaft. (3) Mines office and temporary hospital. (4) New diamond drill—never completed. (5) Original diamond drill hole.

that in an hour we would send down a rubber tube, hoping they could secure the end and drag the slack to a drier part of the mine. Judging from the time elapsed between call and answer we concluded that there must be great difficulty in making the trip to the end of the hole. (Afterward we were told by Mr. Seadding that the pipe came through $7\frac{1}{2}$ feet below and along the wall of an old dam over which the water flowed continually. Also there was a continuous jet of water issuing about the end of the rod itself, so that whoever emptied the rod or gave messages was compelled to stand under an icy shower-bath.)

We ordered 180 feet of garden hose from

of the drill. We lowered away 150 feet, and then began to pour nourishment. First a pail of coffee laced with brandy and glucose, then tomato soup with glucose and cane sugar, ovaltine, etc.

Now began the period of real anxiety for us, for, tragically enough, the size of the hose practically stopped any intelligible conversation. Did they have the hose, or was the slack lying in the mine out of reach? Would all the food so urgently needed simply add to the water accumulating in the shaft? We had temporarily destroyed their life-line, their one connection with the outside world. Were we simply adding

to their mental anguish while accomplishing no good at all?

Every two hours we poured down various forms of liquid nourishment. Then the danger became too great. It was decided to pull the tube up. It would come up about six feet and no further. Was it secured by those whom we were trying to aid, or was it catching on the jagged edge of the diamond drill hole? I shall let you imagine, if you will, our mental searchings of the next hour. Three lives were at stake. The miners might not get there for days. Then it was decided to put compressed air through, so that whether they had the tube end or not they would hear and answer the signal. At last! "Have you got the tube?" "Yes." "What do you want?" "Some soup." (Later Dr. Robertson told us that he would really rather starve than eat our alleged cooking!) Mr. Scadding said that for each pail of boiling liquid they got about two or three pints of icy material, which he was kind enough to say was "first-class". First-class what? we had not intestinal fortitude enough to ask. For six more hours we carried on. Then came the signal followed by a muffled but insistent demand to take up the hose. We felt badly but could not but comply. Then came the news Magill had died. They refused to have the hose down again, but asked for the rods with candles, flash-lights and more food.

By this time a representative of the Maritime Telephone and Telegraph Company had arrived with a miniature one-way telephone, one inch in diameter, which could be lowered down the hole. It was only from them to us, but we felt they could get great satisfaction from that, and we could make some shift down the hole by voice. We told them, "One last load on the rods and then the telephone." "Had they water?" "Yes." "All right, signal. Rap thrice on the rods when you have unloaded. All goes well on top, and we are surely coming through to you. Good luck for now."

Down went the rods with candles, flash-lights, matches, chocolate, coffee and brandy, and finally a note as to how to unwrap the telephone. I think we all felt a little queer as the rods came up for the last time. Nothing could go down after the precious telephone wire.

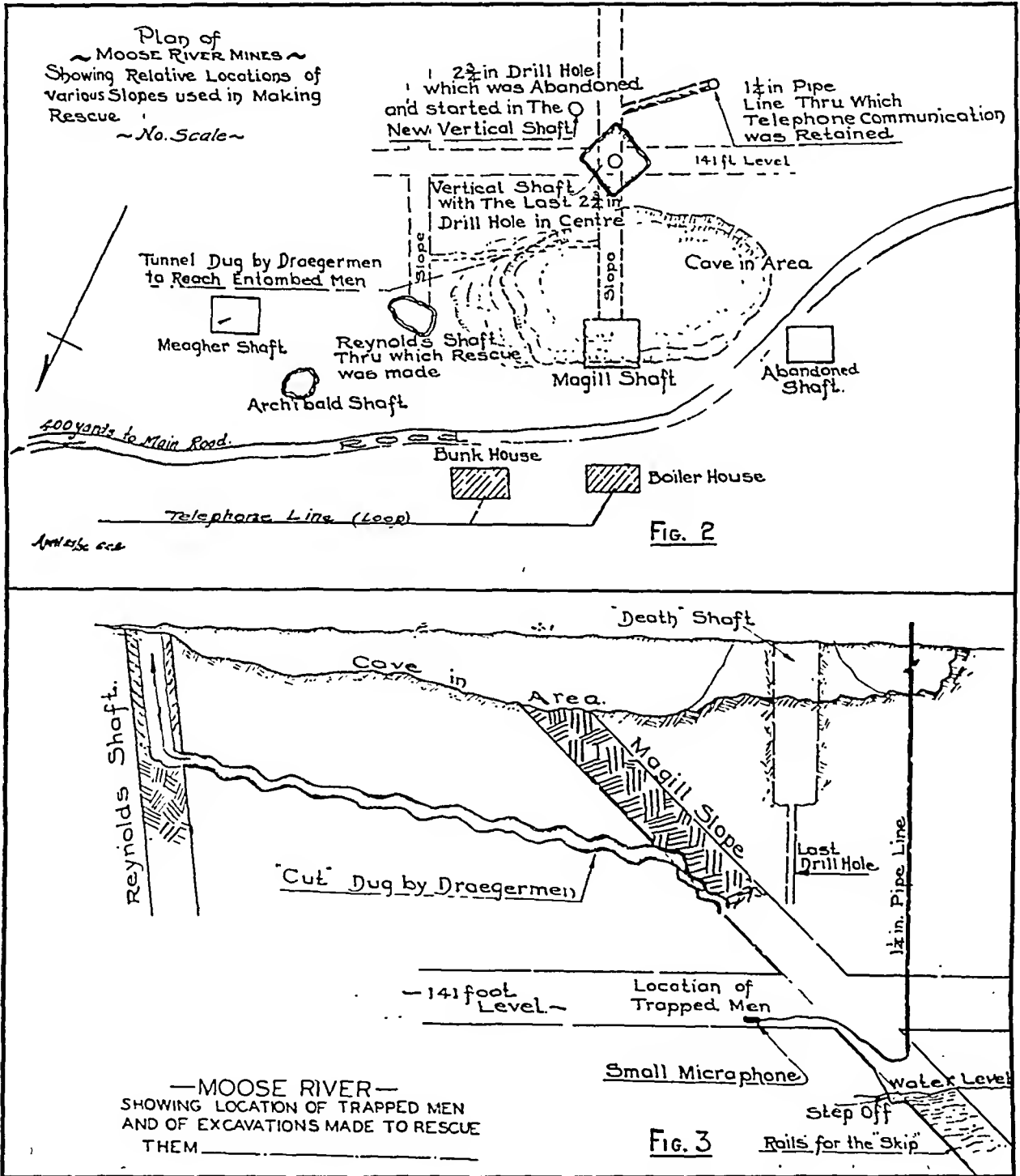
The telephone expert worked like a genius. He had but arrived as the hose came, and he had his wire to straighten and insulate—with a finger of a rubber glove, adhesive tape, and

special waterproofing. At last all was ready, and guided by an iron leader, the best of all gifts from the surface began its perilous journey to the mine chamber many feet below. The receiving set was connected, and the telephone man sat listening to the scratches as the 'phone slid down the drill hole. A pregnant period of silence, and then a clear voice saying: "Hello, is Charley Ivey there?" (Charles Ivey is Dr. Robertson's brother-in-law.) We might interrupt the narrative here to explain briefly what transpired between the time that the diamond drill broke through and the first answer came up from below. This I got from Mr. Scadding after we came to Halifax. Apparently he saw the end of the drill rod and thought it the broken end of an old air line. Later when a flare was let down he thought some dynamite had ignited—hence their reluctance to go near that part of the mine again. Finally the lighted flash-light told of communication with the outside world. After telephone communication had been established, it was agreed to frame all questions from below in such a way that they could be answered, "yes, yes," or "no". Thus the men below could tell from the double or single sound whether an affirmative or negative answer was intended, even though from a distance the spoken word could not be distinguished.

My work as far as the entombed men themselves were concerned had reached an impasse. Until the miners broke into the mine chamber where Robertson and Scadding were living, one could do nothing more for them. Perhaps I might digress for a moment and give a sketchy idea of the rescue operation itself. The sloping shaft which collapsed was near the middle of extensive sloping workings extending 400 or 500 feet on each side of the shaft. These workings also collapsed. Two open shafts which penetrated these workings became blocked at this time, so that there was no open approach to the underground workings whatsoever. A consideration of the best mode of entry resulted in an attempt to go down through another shaft known as the Meagher shaft. This shaft, although remote from the old Magill shaft, was part of the workings, and it was hoped on account of this remoteness that the shaft might not be caved-in to any great depth. This shaft was excavated to a depth of 35 feet, and it was then realized that further progress was impossible due to the extensive weight of the caved-in ground

and the dislosure of the broken and fractured stope below this point. With the arrival of more equipment and more men an attempt was made to excavate the caved-in ground leading down to the original sloping shaft, the Magill shaft. An attempt also was made to sink another shaft in the solid ground away from the eaved-in area, and this shaft actually was put down to a depth of 35 feet. This work was discontinued when it was found possible that the men might be rescued *alive* through other means. Conenrrent

with this work an examination of the fractured ground dislosed an opening from the old workings to the surfaee, which showed some promise of depth: this opening was about 100 feet to the east of the Magill shaft, and was within the caved-in area. When this opening was enlarged it was found that it would be possible to gain entrance to the Magill workings, and the work was prosecuted in the hope that these workings might be opened enough to lead down to the entombed men. At a depth of 35 feet it was



found that these workings were also badly collapsed and fractured, but the work continued, because by this time this method was regarded as the last hope. This opening came to be known as the Reynolds shaft.

All efforts now were concentrated in the Reynolds shaft to gain depth to the westward. The work consisted of the removal of broken rock and the shoring up of their slopes with timber so as to maintain the opening. A chain of men lined the shaft, passing rocks by hand from the working face to the surface. An entry was made into what was identified as the Magill shaft at a depth of 75 feet, and from this point the Magill shaft track rail was followed through the broken and caved-in rock down the slope to a point less than 10 feet above the level where the trapped men were waiting. The total range of caved-in and broken ground through which this opening was made was nearly 200 feet. All of this work was done by hand: it was not possible to use equipment, not even a pick-axe. It was impossible for more than one man to work at the face at one time, and it was necessary for this man to timber his excavation as fast as he made it. The men at the face were skilled timber men, and were relieved every six hours.

In the late afternoon of Wednesday, April 22nd, the Hon. F. R. Davis, Minister of Health for Nova Scotia, Hon. Michael Dwyer, Minister of Mines, accompanied by draegermen, descended the shaft equipped with a specially devised sling apparatus to bring the entombed men up. Dr. W. E. Gallie, of Toronto, Dr. Glen Donovan, Dr. Ian Macdonald, Dr. Rankin and myself were waiting at the surface.

When reached, the physical condition of the entombed men was such that no medication was used until they reached the temporary hospital. Dr. Robertson was able with little assistance to make his own way to the surface, crawling on his hands and knees for the greater part of the distance. In fact, once on the surface, he insisted on walking the short distance to the ambulance stretcher. He was then placed in the ambulance and removed to the emergency hospital which had been set up at the mine office. The ambulance then returned to the mouth of the shaft for Mr. Scadding, who shortly arrived at the surface, and was likewise transferred to the hospital. The state of Mr. Scadding's feet was such that he had to be assisted practically the whole way.

Both patients were undressed, Scadding with the greater difficulty, on account of his swollen feet; woollen combinations put on, and both men were placed in previously-warmed beds. In a very short time those in attendance were struck with the marvellous physical condition of both men. Half an hour after their arrival at the hospital the physical conditions were as follows:

	<i>Dr. Robertson</i>	<i>Mr. Scadding</i>
Temperature	99.6°	102°
Pulse	96	100
Blood pressure	135/80	155/90
Respirations	22	20

Scadding's chief complaint was the condition of his feet, and on examination they were found markedly swollen, cyanosed, and no pulsation in the vessels of the feet could be made out. The feet were cold to touch and there was a definite loss of sensation. His general condition was fair, although the urine contained acetone, 3 plus. A few hours after Mr. Scadding's rescue, in consultation with the doctors present, we decided the condition of the feet was so serious that hospital treatment was urgently required. A plane conveyed Mr. Scadding from the scene of the disaster to the Victoria General Hospital.



Fig. 4

The further course of the case is interesting. On April 25th one Pavaex apparatus (passive arterial exerciser) arrived from Montreal by plane, was immediately applied, and was kept in constant use for the first 24 hours, alternating one leg with the other at three-hour periods. At the beginning the cycle was set for 30 seconds, with a positive pressure of 18 and a negative pressure of 20. As the condition of his feet improved, the cycle was increased to 15 seconds and the positive pressure raised to 25 and the negative pressure to 24. Seadding's complaint was primarily of the noise and vibration of the motors, rather than any sense of discomfort in his feet and legs from the use of the machine. A second machine arrived on April 26th, and this enabled us to treat both feet simultaneously. On April 27th an ultra-short wave diathermy machine arrived, and was used daily in conjunction with the Pavaex appliances. The patient reported considerable comfort from this in that "it warmed his legs up well". After the institution of the Pavaex machines immediate definite improvement was apparent in the superficial circulation of both feet, particularly the right foot. The cyanosis rapidly disappeared, the swelling markedly diminished, and at the end of ten days pulsation in the anterior tibials could be felt. It was considered that the danger of the loss of his feet *in toto* had been pretty well eliminated, but a gangrenous condition of the toes, with a definite line of demarcation at their base, gradually developed (Fig. 4). His general condition throughout was satisfactory; ingestion and elimination quickly returned to normal. From the outset he slept well, and any pain from his extremities was easily controlled by moderate

doses of codeine and aspirin by mouth. The gangrenous process was a dry one. At no time did infection complicate the picture. We are now awaiting the dictum of Nature as to when to operate. It is only too apparent that he will lose all the toes on both feet, but it is hoped that there will be sufficient living tissue so that he will be able to walk in comparative comfort.

Dr. Robertson also complained somewhat about his feet, but apparently they were not in any such serious condition as Seadding's. Some twenty-four hours after his rescue Drs. Gallie and Ian Macdonald became concerned as to his gastro-intestinal condition. He had vomited twice and there was some spasm in the left hypochondrium. They considered it advisable that he should be removed to Halifax, and this was accomplished by plane as in the case of Seadding. From the day of his arrival at the Victoria General Hospital his progress was comparatively uneventful, and he was able to leave by train for Toronto accompanied by Dr. Ian Macdonald on Tuesday, May 5th.

In conclusion, one may say that the outstanding feature to us was the remarkable physical condition of both these men at the time of rescue, and their amazing convalescence. It might be noted that they report, in common with the professional fasters, no desire for food during their incarceration. The initial hunger period apparently was obviated by the unusual circumstances in which they found themselves. Water, fortunately, of good quality was abundant; in fact, too much so. Not a little of the credit for the present satisfactory state of both these men is due the excellent nursing care which they received.

INFLUENCE OF HEREDITY ON SYSTOLIC BLOOD PRESSURE.—V. Augustin reports from the University Hospital of Budapest investigations conducted between 1923 and 1932 into the possibility of a relationship between the blood pressure of parents and that of their children. In 8,805 cases patients were questioned as to the cause of death of their parents, and their age at death. The blood pressure of the patients themselves was measured by a Riva-Rocci-Recklinghausen instrument in the recumbent position. The sex as well as the age of the dead parents was noted, and in each case the cause of death of only one parent was taken into consideration. The causes of death were classified accord-

ing as they were due to such conditions as hemorrhage into the brain, "heart paralysis", arteriosclerosis, diabetes, and disease of the kidneys. It was found that the blood pressure of the offspring of parents dying from one or other of these diseases was comparatively high on the average, whereas it was comparatively low in the case of patients whose parents had died from tuberculosis or some disease of the stomach. An intermediate position was occupied in the case of the patients whose parents had died from cancer, old age, or pneumonia. Augustin considers that a case has thus been made out for considering heredity as a factor in the determination of the blood pressure.—*Deut. med. Woch.*, March 6, 1936, p. 388. Abs. in *Brit. M. J.*

THE EFFECTS OF PRIVATION IN THE MOOSE RIVER MINE DISASTER

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THE details of establishing communication with the men trapped in the Moose River Mine have been sufficiently dealt with by Dr. H. K. MacDonald in the present issue. The present account will be concerned only with the effects produced by cold and starvation in one of the survivors, Dr. D. E. Robertson.

After Monday, April 19th, everything spoken into the microphone was recorded at the surface, and thus important information became available about the physical condition of the men. They were cold and wet, their feet were badly swollen, they had distressing gastro-intestinal disturbances, and they suffered such severe discomfort and pain that it was difficult for them to rest in one position for more than a few minutes at a time. They had an abundant supply of water. Mr. Magill the youngest of the three, it was now known, had died from exposure and not from trauma. Mr. Scadding declared three days before the rescue that "he could not walk ten feet without falling". Twenty-four hours later Dr. Robertson intimated that "the situation was miserable". A few hours later Mr. Scadding added "my legs are paralyzed from the knees down, they feel like blocks of wood, and I can't move them, or feel them, or walk any more". During the last twenty hours before the rescue bits of the conversation below were heard above, and the fear increased that the two men were dangerously weak and that Mr. Scadding's legs were in a grave condition. When rescue became imminent there was growing anxiety as to whether they had sufficient vitality to withstand the handling necessary to carry them up through the narrow, tortuous tunnel, to the surface. But the limits of human endurance cannot be estimated, and the tensely waiting crowd were astounded and delighted to see Dr. Robertson emerge from the pit head practically without aid, while his younger companion was carried out in a better condition than had been hoped for.

Recorded observations on the effects of inanition and cold on the human organism are very important, and therefore the findings on ex-

amination of one of the survivors (D.E.R.) of this terrible ordeal will be referred to somewhat in detail.

His face was blackened with grime and covered with ten days' growth of beard. His expression, while drawn, was nevertheless bright, and he was alert and cheerful. After his face had been cleaned it was observed that a hectic malar flush was present, and that there was a considerable amount of wrinkling about the eyes and mouth. Emaciation was not evident. The breath was neither foul nor sweet. The tongue was moist, red, slightly swollen, cracked and tender. Several inflamed-looking, tender plaques, were present on the dorsum. He complained of spasm in the throat and a sensation of burning beneath the sternum. It was observed subsequently that he suffered from intermittently recurring spasms referred to the region of the epiglottis, the pain being very intense for periods up to a minute and accompanied by stridor. The heart rate was 108 per minute with regular rhythm. The pulse was quite forcible. The blood pressure was 135/84. There was no demonstrable cardiac enlargement and no murmurs were noted. The respiratory rate was 23 per minute, the movements being rhythmical and of moderate depth. No sighing was observed. A moderate number of moderately coarse râles were heard at the right base posteriorly and in the axilla. The abdominal wall was slightly retracted and there was a slight degree of rigidity in the right upper quadrant. No tenderness was present. The pupils were moderately dilated and reacted briskly with direct and consensual light and with accommodation-convergence. The knee and ankle jerks were present and equal. Chvostek's sign could not be elicited, but Trousseau's sign was present.

The hands were swollen, badly cracked, rough, cold, and tender. The tips of the fingers were of a greyish blue colour, while the remainder of the hands were of a reddish tint. Appreciation of light touch was impaired over the fingers and palms and sensation to pin prick was slightly

dulled. The feet and legs were swollen. The feet were of a greyish blue colour and there was a small dull red area on the plantar surface of the left great toe. They were cold and tender, and numbness was complained of. There was good pulsation in the dorsalis pedis and posterior tibial arteries. Sensation to light touch was considerably impaired over both feet; pin prick was appreciated quite well except over the larger part of the great toes and the tips of the other toes; and deep pressure sense was defective over the anterior portions of both feet. A small pressure sore was present on the left buttock.

He had been placed in bed between blankets and surrounded with warm bottles before the examination had been made. Soon after walking to his bed he asked for dry toast and tea and both had been given to him. When he first took fluid he retched a bit. A warmed alkaline mixture was then given with the object of relieving some of the burning present in his throat and beneath the sternum. During the night it was found that a few drachms of this solution would allay the distress in the throat. The pulse and respiratory rates rose slightly during the first three hours to 112 and 23 respectively; but by 8.30 a.m. the pulse had fallen to 100 and the respirations to 20. The temperature was 98.6° (axilla) at 3.20 a.m. while at 6.50 a.m. it was 99.4°. Urine voided about 3.30 a.m. was found to be alkaline in reaction and to contain no acetone bodies.

Sleep, as noted, was disturbed and the short waking periods were utilized to administer fluid. Clear warm tea, sweetened with two or three teaspoonfuls of sugar, proved to be a most acceptable drink. Hot and cold fluids were painful to swallow; and orange juice could not be tolerated for the same reason. During the first eight hours he took about thirty ounces of fluid and he derived a considerable amount of comfort in the chewing small pieces of crisp toast.

About 3.40 a.m. he awakened and complained bitterly of feeling very hot although he had no increase in temperature. Within a few minutes he became nauseated and made an unsuccessful attempt to vomit. He then dozed for several hours and was awakened about 6 a.m. suffering with crampy abdominal pain. At intermittent intervals he had complained of numbness of the feet. Just before 7 he commenced to suffer again from painful spasms in the throat and calcium

gluconate gr. 60 was given in a successful effort to relieve him. The only other drug given during the night was phenobarbital gr. 1/2. No fluid was given intravenously and no insulin was given. At daylight the malar flush previously referred to became more evident and it was noted that there was a diffuse blush over the entire body. This could be made to disappear with pressure but it re-appeared slowly, taking two minutes to recover its previous intensity.

During the day following the resene his feeling of well-being improved rapidly and he called for increasing amounts of fluid. However, towards evening he was not quite so well, and as the night progressed he suffered intermittently from epigastric pain as well as from spasmodic attacks of pain in the upper part of the throat. He vomited a bile-coloured fluid on two occasions and was nauseated on several others. The next morning, April 24th, it was considered advisable to remove him to hospital and this was accomplished comfortably through the splendid cooperation of the R.C.A.F. Re-examination after arrival showed a considerable degree of improvement. Blood was taken for chemical examination; the blood sugar was 0.105 mg per cent; CO₂ combining power 70 volumes per cent; creatinine 1.68 mg.; urica 16.4 mg.; and non-protein nitrogen 35.2 mg. During this day vomiting became troublesome and frequent feedings were commenced with a thick mixture containing milk, lactose and cereal. This was retained successfully, and from this on there were no further worries about his diet. No solid food was given until April 28th when he relished a small steak. After this there was a rapid increase in appetite and for the next two weeks he was almost voracious. His general condition showed a remarkably rapid degree of improvement after the fifth day. This observation is in accordance with those made in different experiments on the subjects of prolonged fasting.

The sequence of changes observed in the skin and in the extremities was of considerable interest. The first examination, made under lamplight, had revealed a slight blush over the back and chest. At daylight this was seen to be of a pinkish colour, most marked over the trunk. The blush could be made to fade with pressure and the imprint of a hand remained white for about thirty seconds and did not match the surrounding colour for two minutes. The cheeks, hands, and feet were of a deeper colour. The

appearances suggested those often seen following histamine injections. During succeeding days the skin lost its hyperæmic appearance gradually and areas blanched by pressure required less time to regain their colour. On April 28th the imprint of a hand on the back disappeared in twenty seconds, while there was no mark on the abdomen after fifteen seconds. No *tâche* was observed. On May 1st slight, fine desquamation commenced over the trunk, while quite large flakes peeled from the hands. Desquamation seemed to be complete over the trunk in about ten days while the hands and feet peeled for a longer period. Evidences of hyperæmia of the skin persisted for about two weeks after removal from the mine. This appearance was considered to be due to vasomotor imbalance and it is of interest to recall that one investigator of the effects of starvation concluded that the vasomotor effects which he observed were due to damage to medullary centres.

The hands changed in appearance during the first twenty-four hours, a definite purplish blush becoming evident. The tips of the fingers soon commenced to tingle, and there was also some tingling of the palms. The hands felt thick, boggy, and warm. There was some distension of the superficial veins of the forearms. On April 28th it was noted that the blush over the hands, which had disappeared temporarily, had become more marked, and that a distinct difference could be noted between the temperature of the hand and of the cooler forearm, the line of demarcation being quite sharp just above the wrist. The nails were yellow with longitudinal ridges and the nail beds seemed to be ischæmic. The skin of the hands remained rough and boggy for about a week and a small sore became evident on the tip of the right middle finger. Appreciation of light touch was impaired to a marked degree for two weeks but pin prick was definitely painful and sense of position on passive movement was not affected at any time.

The feet were involved in a most troublesome way. The brawny swelling noted at first soon commenced to recede and the greyish purple colour changed to a purplish red within a few hours. There was a small scarlet area on the plantar surface of the left great toe, and the nails of both great toes were discoloured by underlying hæmatomata. The *dorsalis pedis* pulsations were easily visible and palpable at all times, while the posterior tibial pulsations were

strong. The numbness present in the beginning disappeared to a certain extent with subsidence of the swelling, and was followed after a week by intermittent attacks of severe, lancinating pain, as well as sensations of heat, cold, and tingling. On the third day Dr. Robertson complained of the feet feeling as if they had been peppered and that they were very hot. Examination at that time revealed bounding pulsations of the *dorsalis pedis* arteries, distension of the superficial veins of the legs, and reappearance of the red blush. The feet felt quite warm to the touch, and a sharp change to a lower temperature could be detected at the ankles. Twelve hours after this further changes were noted. On lowering the feet for a minute a purplish blush became evident on both feet anterior to a line extending across the mid-tarsal joints. These changes could be followed in decreasing degree for several days. There was tingling, with intermittent attacks of sharp pain radiating forward from the soles to the great toes for some weeks. Movement of the great toes was very painful for the same time. He commenced to hobble about his room on the seventh day but every step was painful. There was less pain after he commenced to wear boots. Difficulty in walking persisted in decreasing degree for six weeks, due, it was believed, to ischæmic neuritis of terminal twigs.

The urine was examined each morning for a week and was found to be alkaline in reaction on every occasion. Acetone bodies were not present and microscopical examination revealed no abnormalities.

The temperature changes differed from those observed in fasts uncomplicated by exposure. These latter were found to be accompanied and followed by subnormal temperatures; while in this case there was a low grade fever for about a week. The cause for this could not be established definitely, but it was most probably due to the peripheral-vascular changes and not to the slight degree of congestion present at the base of the right lung. The pulse was accelerated, and ranged between 90 and 98 during the first week. The blood pressure which was 135/84 on April 23rd was 118/70 on April 26th, and 128/78 on April 28th. The weight lost was difficult to estimate. No chair scale was available and he had to be supported when standing on a platform. However, it was calculated that there were about

fifteen pounds lost. There was no special degree of emaciation.

The throat continued to be troublesome for several weeks. It is probable that there was some superficial ulceration of the œsophagus, as certain foods caused pain, while hot and cold liquids could not be tolerated.

The story told by the patient during the few weeks following the rescue contained many points of medical interest.

Vomiting had affected two of the men within eighteen hours of the cave-in and it continued to be present at intermittent intervals during the remainder of the time they were in the mine. The vomitus was profuse and very sour and burning; and on many occasions it flowed up with very little effort. The cause for this vomiting is difficult to explain. The water, which they obtained from a pipe, was hard "gold" water. Unfortunately a specimen could not be obtained for analysis but it is usual for water of this type to carry considerable amounts of mineral salts. It is possible that the vomiting was initiated by the drinking of too much water, and it is also possible that it resulted from psychological reactions. I believe that it is probable that the wood smoke which filled the mine for many hours produced a slight asphyxia which was sufficient to act on the vomiting centre. I do not believe that acidosis severe enough to cause vomiting could have resulted as early as eighteen hours. By means of this vomiting large amounts of acid were lost from the body. One wonders if the damaged tissues of the extremities released H-substance into the circulation in sufficient quantities to serve as a continuous stimulus to hydrochloric acid production in the stomach.

It is of interest to note that hunger never troubled the men during the ten days they were without food.

CONCLUSIONS

From the data given certain conclusions have been drawn as to the effects of inanition and

cold on the human organism. It is evident that the "margin of safety" of the human machine is very great and that starvation can be combated by mobilization of body reserves. In this instance cold was a factor; is it possible that the stimulus which it afforded to metabolism was of assistance in enabling the body to draw upon its reserves more easily than it could have done otherwise? This patient was the oldest of the three men who were entombed; and he was the fattest and the one whose occupation was the most sedentary. He nevertheless withstood the gruelling ordeal better than the others, and it is probable that he was able to do so because of his stores of "mobile" fat.

The changes observed in the skin and in the extremities were considered to be due to vaso-motor imbalance. This was not considered to be associated with the metabolic disturbance although a previous experiment on fasting had produced evidence to show that starvation caused a certain amount of vaso-motor instability due to central action.

Thirty years ago F. C. Benedict noted that the mental attitude of the fasting subject determined in a large degree his ability to withstand a fast; and there can be no doubt that the psychological reactions of this patient and his companions served them in good stead during the ten days of their travail.

SUMMARY

1. The history and findings on examination of a man exposed for ten days without food in a cold, damp, mine are recorded.
2. The findings differed in many respects from those recorded in experiments on fasting.
3. There were no signs of acidosis. Mild tetany was present.
4. A series of vaso-motor changes were observed, more especially in the feet.
5. The limits of human endurance are difficult to estimate, but would appear to be increased when adequate body fat is present.

RECENT PROGRESS IN SEVERE DIABETES*

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INTRODUCTION

THE past five years have completely changed our conception of the etiology, physiology and therapy of diabetes. They have revealed new complications, given us a new race of long-duration young diabetics, and even changed the eventual prognosis of the disease. To the solution of these problems the severe diabetic has contributed much, and from this newer knowledge he, in turn, has received the greatest share of the benefit.

Etiology.—The newer research in the fundamental etiology of diabetes indicates to us that all cases of diabetes are genetic and possibly pituitary in origin. The actual proof of the hereditary nature of diabetes belongs to recent years, for the duration of life of the diabetic was so short prior to insulin therapy that the data of family histories could never be complete. Since there is a certain amount of disagreement concerning it, I wish to review briefly our own investigation of this problem.

The actual evidence in favour of the theory that the potentiality for developing diabetes is inherited rests primarily with four facts:¹ first, the almost simultaneous occurrence of diabetes in similar twin mates; second, the greater incidence of diabetes in the members of a diabetic than in a control family; third, the demonstration of Mendelian recessive ratios in a large series of cases selected at random; and, fourth, in presumably latent cases.

Of similar twins, the most valuable material for the student of human genetics, we have a relatively large series, thirteen pairs. A comparative analysis of similar and dissimilar twins in our own series gives striking evidence in favour of the genetic origin of diabetes. Thus, in 70 per cent of our similar twins both twin mates have contracted diabetes, compared

with only 12 per cent of our dissimilar twin mates. Diabetes was found to occur nearly seven times more often in the parents and siblings of diabetics than in the relatives of our non-diabetic patients, and this is a statistically significant difference.

All of this suggests, but does not prove, the hereditary nature of diabetes. To be convinced, we must know even more. We must find and demonstrate the mode of transmission. Here it is that students of diabetes disagree, some finding no pattern, others simple dominance, double dominance, or alternating dominance and recessiveness, or simple recessiveness. For a moment let us review the Mendelian hypothesis. It presupposes that inherited traits occur in pairs and in opposites, in our problem—diabetics and non-diabetics. Second, that the traits of parents with unlike inheritable characteristics generally do not blend, but one tends to recur in the offspring and is dominant, and the other tends to disappear and is recessive. Third, and the most important in a problem such as ours, is the fact that the traits of offspring of parents possessing unlike inheritable traits can be predicted according to certain ratios. In a series of consecutive cases we believe that we were able to demonstrate Mendelian recessive ratios. According to this pattern, in a cross between two diabetics we expect 100 per cent of the offspring to become diabetic; in the cross between a diabetic and an hereditary carrier, 50 per cent; and in a cross between hereditary carriers, 25 per cent.

Certain factors, however, alter our expectations. First, the mode of selection of these families will do so, for it is true that they were chosen because there was a known diabetic. This is the only method of determining carriers in the study of human heredity. A known mathematical correction is permitted for this,

* A paper read before the Hamilton Academy of Medicine on January 15, 1936.

and it lowers our expectations to 100 per cent, 40 per cent, and 16 per cent in the three crosses, respectively.

The age behaviour of diabetes lowers the expectation of fulfilled ratios further. It is known that the onset of diabetes occurs anywhere from 0 to 90 years of age, with a peak of incidence at 50. Third, the ordinary chances of death from extra-diabetic causes, such as tuberculosis, typhoid fever, or automobile accidents, will actually destroy 50 per cent of predestined cases prior to any possible identification of the disease. Thus, it is improbable that the relatives of diabetic patients can attain that age, 90 years, which would completely fulfill our simple Mendelian expectation of 100 per cent, 40 per cent, and 16 per cent in the three crosses, respectively, and at any given moment of study we will find only a fraction of fulfilment.

What fraction did we find? We found that 24 per cent of the offspring of our diabetic-diabetic cross have developed diabetes. We expected 100 per cent, so this was almost exactly one-fourth. We found that 10 per cent of the offspring of our diabetic-carrier cross had contracted diabetes. We expected 40 per cent; again this was one-fourth. We found 4 per cent in our offspring of carrier-carrier cross. We expected 16 per cent, so here again we have identified one-fourth. But the expected and identified ratios were almost identical, for 16, 40 and 100 are the ratio of 1:2.5:6.1 and 4, 10, and 40 in the ratio of 1:2.4:5.7. Even this analysis is subject to criticism because it is based upon the case histories, so that we actually tested 294 individuals, 169 close relatives of diabetics and 125 controls by sugar tolerance tests and random blood sugars. Supernormal blood sugars, statistically supernormal, were found in 25 per cent of the diabetic relatives and in 2 per cent of the relatives of our control population. Significantly abnormal blood sugars were found to occur in nearly true simple Mendelian recessive ratios of 1:2:4.

This leaves our problem, the search for the fundamental etiology of diabetes, only half solved. Given the proper genetic background, what determines that it shall be expressed as diabetes, for no genes operate *in vacuo*? Endocrine functions are known to be controlled by Mendelian recessive genes; for example, dwarf-

ism in mice, and probably the human cretin.

As Houssay² has suggested, two possibilities exist, namely, that the gene influences the pancreas through (a) hyperactivity, or (b) hypoactivity of the pituitary. The hyperactive pituitary is theoretically associated with an excess of the diabetogenic factor of Houssay, whereas a hypoactive pituitary is consistent with a lack of the pancreatropic hormone of Anselmino and Hoffman. Evidence of both hyperactivity and hypoactivity can be found in clinical cases of diabetes, but hyperactivity is suggested by the overgrowth which occurred in 90 per cent of our diabetic children prior to the onset of the disease. Further, the age incidence of diabetes is coincident with that of hyperactivity of the pituitary gland, at 6, 12 and 50 years. In contrast to this, obesity in the adult and dwarfism in some diabetic children suggest hypofunction of the pituitary. The hyperactive type is associated with more severe clinical diabetes; the hypoactive type, with a milder form. Whether the precipitating factor is something in the external or internal environment remains to be solved.

DIAGNOSIS

In contrast to the complex problem presented in the etiology of diabetes, the recognition of the disease is extraordinarily simple. Dr. Joslin's criteria for diagnosis are the presence of sugar in the urine and an elevation of blood sugar in the fasting state to 140 milligrams, or in the post-prandial state to 170 milligrams if the blood is venous, and 200 milligrams if the blood is capillary or arterial.

TREATMENT

Many forms of treatment of diabetes have arisen, but the fundamental principles and aims are the same: first, to maintain weight, or, if the patient is a child, to promote the normal rate of growth and development; second, to render the urine practically free from sugar and maintain the blood sugar at normal levels; third, to control fat metabolism; and, fourth, to prevent acidosis.

(a) *Diet.*—The dietary treatment of the disease depends upon its severity and, incidentally, upon the age of the patient. With the average cooperative adult diabetic over 50 years of age treatment has never been too difficult, and the end-results have been usually good. The end-results with a severe and youthful type of

diabetes have been less satisfactory, and as a consequence many different forms of dietary treatment have been used. These concern the partition of the diet into its component parts, carbohydrate, protein and fat, rather than the total calories. Today it is generally agreed by students of diabetes that the average adult over 50 will maintain a normal weight, providing he receives 30 calories per kilogram of body weight, and the child will grow at a normal rate if he receives 100 calories per kilogram during infancy, gradually decreasing to 45 calories per kilogram during adolescence and 35 per kilogram through active early adult life. Every possible variation of carbohydrate, protein and fat has been advocated for the youthful and severe diabetic. There are advocates of low-carbohydrate and high-fat ratios; moderate-carbohydrate and moderate-protein and moderate-fat; high-carbohydrate and low-fat; high-protein and low-protein. The real defeatists are proponents of the free or normal diet. For our own part, we have had the happiest end-results when for the adult patient the carbohydrate has varied from 150 to 200 grams, and for children from 150 to 250 grams, and for the latter 2:1 or 3:1 carbohydrate-fat ratios.

Desugarization of the severe diabetic is facilitated by the collection of specimens at nearly two-hour intervals. Qualitative tests are done upon nearly all of these specimens, but only the pre-meal and retiring tests are of value in treatment. We test one day to determine the adjustment of insulin for the following day. If the 11.30 test is poor one day, then the morning dose of insulin is increased the following day. Besides these qualitative tests, quantitative determinations are made upon the twenty-four hour amount and blood sugars are done at weekly intervals. Preferably all these analyses are made on a single day so that we have a picture of the patient's sugar metabolism for an entire twenty-four hours.

(b) *Insulin*.—So far as insulin therapy is concerned, we are in a transitional stage. The problem of the amount of insulin for a new patient can unfortunately not be solved by mathematical precision. Our rule has been to give small doses of insulin in childhood and old age. Under 5 years we start with 3 units three times daily; between 5 and 10, 5 units three times a day; and between 10 and 15, 10 units three times daily. This is changed each day by

the method of trial and error, and at discharge administered twice daily.

(c) *Protamine insulinate*.^{2, 3}—The new protamine insulin or Danish insulin retard, however, will revolutionize therapy, and the severe diabetic will profit most. After three years of the disease, all youthful and severe cases show an elevated fasting blood sugar, well over 300 milligrams. From the third year of duration on the blood sugar becomes stabilized. There is no tendency for increasing severity of diabetes indicated by increasing fasting hyperglycæmia. To counteract this most students of diabetes have prescribed either a dose of insulin between 10 o'clock and midnight, or one at 5 o'clock in the morning. The first method of treatment has resulted in an abrupt fall of the blood sugar at hypoglycæmic levels followed by a spontaneous rise, so that even with this extra dose of insulin the fasting blood sugar was relatively high. Insulin given at 5 o'clock in the morning or earlier controls night hyperglycæmia, but is inconvenient. Various attempts have been made to reduce this rapid absorption of insulin (the fundamental defect of our present therapy). Clausen suggested that it would be wise to combine insulin with vaso-constrictors. We tried this with a few of our patients but the results were not striking. Leyton, of London, suggested an oily suspension, but produced abscesses instead of retardation of absorption, and Bertram reported good results by combining insulin with protein. However, this work was never followed. For several years Doctor Hagedorn has worked upon this hypothesis. If insulin is combined with a base, injected as a suspension the minimum solubility of which occurs at the hydrogen-ion concentration of body fluid, the precipitate will be slowly broken down and active insulin released in small quantities over a long period of time, more nearly simulating the insular secretory function of the normal pancreas. In order, he tried the tri-, bi-, and the mono-protamines, and found that a new one, a mono-protamine which has never been described in the literature, derived from the ripe sperm of the American *Salmo iridius*, provided the minimum solubility at the desired hydrogen-ion concentration, 7.3 compared with 7.7 of our regular insulin hydrochloride.

For two years Doctor Hagedorn has been using this in Copenhagen. Our first experi-

mental lot came to us in July, 1935, and we had an opportunity to use it with 19 patients. Our own work has been merely to confirm the results reported by Hagedorn. This insulin remains in the body nearly twice as long as ordinary insulin. The drop in blood sugar is very gradual, and insulin reactions are reduced to the minimum. Protamine insulin will not replace the regular insulin. Because of its slow absorption it is not of great value in crises such as diabetic coma or infections. It may not replace regular insulin entirely even in the treatment of severe diabetes. At first, the best results were obtained by using the regular insulin in the morning, when we want rapid action, and insulin retard in the evening. By so doing there is just a gradual fall of blood sugar and the patient awakens with a normal fasting blood sugar. More recent experiments indicate that complete replacement is possible. As a result of this new therapy we believe that some of our severe juvenile patients who are now taking insulin four or five times daily will be able to reduce the frequency of injections to twice daily, and milder cases using insulin two or three times to a single injection. No harmful local or general reactions have been produced either in the laboratory animal or the diabetic patient. We are very enthusiastic about this and believe that it will revolutionize the treatment of the juvenile diabetic. Further, since one substance has been discovered others will be found, and the treatment of diabetes may become as simple as that of pernicious anaemia.

Complications. — Today there are people among the laity and especially diabetic patients who believe that the treatment of diabetes does not pay. We are particularly antagonistic to this attitude; we know that the sequence of events in severe untreated diabetes is (1) the interurrence of the crisis, coma; (2) the loss of weight and strength, or failure of growth; (3) the loss of resistance to infections, and death from septicæmia; (4) premature ageing.

1. Diabetic acidosis still occurs with great frequency in the severe diabetic. Insulin has changed the prognosis entirely, reducing the total mortality of coma from nearly 100 per cent to that of 14 per cent of our entire coma series of 317 cases, and to 0.7 of 1 per cent in our patients who had onset of diabetes under 15 years of age. At the George F. Baker Clinic of the New England Deaconess Hospital, between 1923 and

1935, 134 cases of coma in patients with onset of diabetes in childhood have been treated with but one fatality.

To the etiology of coma—diet-breaking, omission of insulin, infection, disease of the glycogen storage bodies (i.e., extensive disease of the skin, liver and muscles) — we can now add a new factor, endocrine imbalance. This has also been observed by Bertram. It is suggested by the greatly increasing frequency of the incidence of diabetic coma during pregnancy and catamenia. The type of acidosis which occurs during pregnancy and during catamenia is characterized by a relatively low alkali reserve and also a low blood sugar which may be as low as 190 milligrams. This is merely to warn against the interurrence of acidosis during pregnancy, and particularly to warn patients of the extra care and the readjustment of insulin which may be necessary at the time of catamenia.

The treatment responsible for recovery of 86 per cent of our cases has been (a) insulin in large and divided doses, ranging from 10 to 1,000 units given in the first twenty-four hours; (b) fluid to combat dehydration, from 1,500 to 8,000 c.c. of normal salt solution, should generally be given in the first six hours; (c) repeated gastric lavage and enemata to counteract loss of gastro-intestinal tone. Concentrated glucose 50 per cent, or concentrated salt solution, 10 per cent, may avert a renal block. Ephedrine, adrenalin, and rarely blood transfusions are used in cases of circulatory collapse, and carbohydrate is given up to 100 grams by mouth in the first 12 hours. Our reason for not giving glucose or alkali parenterally is physiological, that with insulin glucose is set free. It will burn the incompletely burned fat products, thereby releasing base. It is true that with severe acidosis the average rise of the alkali reserve is slow, only 12 volumes per cent in 8 hours, but, with this slow rise, our mortality has been only 0.7 per cent. We have recently been criticized by Hartman for not using alkalis, specifically racemic sodium lactate, but in his series of diabetic children treated with sodium lactate the mortality was 18 times that of ours, namely, 13 per cent. We feel that we cannot change our method of treatment in the presence of so high a mortality rate when we believe that the harm done was not the actual use of the alkali but the false sense of security which is given by the rapid rise of the alkali reserve. The fundamental fault, lack

of insulin, has been overlooked. The amount of insulin which he has advocated, namely, 2 units per kilogram of body weight and none for 6 hours, would be inadequate for our own serious and severe cases of acidosis, who have required up to 17 units per kilogram.

2. Hypoglycæmia, we hope, will be, practically, a problem of the past with the new protamine insulin, although it is perfectly possible to produce an occasional bad insulin reaction with it, because it remains in the body so long. One would anticipate a prolonged series of reactions in case of a maladjustment of a dose of protamine insulin. Severe hypoglycæmia is best controlled by 50 per cent glucose intravenously administered.

3. Skin lesions.—The severe diabetic is particularly prone to the development of skin lesions, which include a newly described one, namely, *neerobiosis lipoidica diabetica*. This appears as red papules from 1 to 3 millimetres in diameter, which are topped by a slight scale and do not disappear under glass pressure. One of our patients mistook them for mosquito bites. Later the areas are round or oval, with well-defined borders, of firm consistency, and have a smooth glistening surface, which looks as if it were covered with a layer of tightly stretched cellophane. Still later, depressed areas with atrophy and ulceration occur. It is believed to be due to fatty degeneration of connective tissue or *neerobiosis* of connective tissue followed by imbibition of lipoids, and is said to resemble the areas close to those of actual gangrene. In our series it has not been associated with a high blood fat; some patients have high blood-cholesterol and other normal values, and it is most usual among patients whose disease has not been under good control. In contrast to this lesion, *xanthoma diabeticorum* is always associated with an elevation of blood fat. Here the lesions are golden papules on a red base and disappear when the fat content of the blood returns to normal levels. Abscesses and carbuncles are prevalent in proportion to lack of control of the diabetes.

4. Dwarfism.—Failure of growth in stature amounting to dwarfism, though an infrequent complication, has been one of our greatest concerns. Whereas 95 per cent of our diabetic children have actually grown and developed normally, 5 per cent have failed to do so. Thus, in our series of 1,063 children there are 54 who

have at some time in their diabetic lives been from 4 to 13 inches below the standard average height for their ages. Dwarfism in our experience has not preceded diabetes; although we do not have the height at onset of diabetes in all, many not coming to us until several years after onset, we have sufficient data to know that the stature was normal or even above height prior to the recognition of this disease. Consequently, we have thought that although the primary fault was undoubtedly functional hypoactivity of the pituitary with lack of growth hormone it was to be related to undernutrition. Houssay, however, has reported a similar case in which there were, at autopsy, scars in the pituitary, and he has pointed out to us that it is quite possible that defective pituitary secretion may be responsible for coincident conditions—lack of pancreatropic hormone producing diabetes, and lack of growth hormone producing dwarfism.

Various methods of treatment have been employed, but largely three: high-calorie and high-protein diet; high-calorie, high-protein diet, with the addition of thyroid and pituitary gland extract; high-calorie and high-protein diet with growth hormone. The over-nutrition diet alone stimulated growth somewhat, but those patients treated with thyroid extract had a better rate of growth. We cannot report upon the results of growth hormone, because this work was started only in July, 1935, but in this short period of time the average rate of growth in four months has been one inch compared with one-half an inch for the normal child, and many of these children have been growing at the rate of less than one-half an inch a year. Some of them have grown almost two inches in this period of time. One of the commercial preparations seems to have a beneficial effect on blood sugar, the other no effect. We were hesitant about using these preparations at first because they are not pure; among other impurities, a diabetogenic factor is supposed to be found with the growth hormone, and it might increase the tendency toward glycosuria, hyperglycæmia, and acidosis. However, none of these children have presented any harmful effects. Then, too, the newer work on the anti-hormone⁶ suggests that the prolonged use of such a substance as growth hormone may in the end retard growth,

but with six months' continuous use no harmful end-results have occurred.

5. Enlargement of the liver.—Another interesting complication is enlargement of the liver, which has been described only recently. This has been observed in 60 of our juvenile cases. This is not an insignificant enlargement, but actually the liver can be felt at the level of the iliac crest, and these patients often present themselves with a protuberant abdomen, due to the tremendously elongated and infiltrated liver. Such patients present serious problems in treatment because they are very unstable and are liable to frequent attacks both of insulin reactions and of diabetic acidosis. The cause of this enlargement has not been clear. Theoretically it may be due either to an excess of fat or to an excess of glycogen deposited in abnormal fashion. Several post-mortem examinations done in more or less complicated cases have shown that the enlargement has been due to fatty infiltration.

Diabetic dogs have been reported by Soskin, Best and Hershey,⁶ and Chaikoff⁷ with enlarged livers, infiltrated with fat. The problem with the experimental animal, however, is not quite the same, because, after all, they have been deprived of the external secretion of the pancreas, but in line with this is the possibility that these diabetic children may have had a congenitally small pancreas with a deficient external factor. Four autopsies have been done in this group, and they do not show small amounts of pancreatic tissue. The pancreatic ferments have been studied also, and a deficiency of lipolytic ferments has been found.

Liver function tests reveal little. However, the ratio of free cholesterol to cholesterol ester has been reported to be low in the experimental animal, indicating that this function of fat metabolism of the liver is defective. The total fat, however, may not be abnormal. As far as therapy is concerned, we have to treat these cases as if all were due to infiltration of fat. Best and Hershey have reported excellent results with the use of cholin, lecithin, or whole pancreas. We have been administering betaine hydrochloride, a choline-like substance. There is an immediate change on physical examination. The liver, which has been thick and readily palpated, can no longer be well defined. There is no change by x-ray in four

months. Untreated, these lesions can be of very long duration. We have observed certain cases for a period of five years. It is interesting here to note that excellent results have also been reported by Hansen with protamine insulin. Whether this alters fat metabolism, or perhaps the storage rate of glycogen progresses in a slower and more normal fashion, one does not know.

6. Degenerative changes.—An analysis of the long-duration case gives a picture of the end-results of severe diabetes. Again we turn to our juvenile series and find that a total of 53, 5 per cent, of our entire juvenile series have survived 15 or more years of the disease. Of this number 49 are living and 4 have died. Nineteen per cent have had coma; 43 per cent, arteriosclerosis; 28 per cent, retarded growth and development; 8 per cent, infections; none, tuberculosis; 6 per cent, cataracts; and 6 per cent, neuritis. This brief summary shows that failure of growth and development and degenerative complications have occurred too frequently. Uncontrolled diabetes is characteristic of the long-duration cases as well as other youthful cases who have developed such degenerative lesions. Prior to 1922 young diabetics did not live long enough to develop such changes. Coma destroyed childhood cases; tuberculosis destroyed young adults. Uncontrolled diabetes is measured chemically in two ways, either by hyperglycemia and glycosuria or by excess of lipids in the blood, and by ketone bodies in the blood or urine. We have tried to evaluate these various factors, and our own conclusion is that an excess of fat is the precursor and, we believe, the cause of degenerative changes. A social survey shows that these children are employed, economically independent, have married and reproduced. This brings us to the consideration of a complication which, more than any other, has not yielded to insulin therapy—namely, pregnancy complicating diabetes.

7. Pregnancy complicating diabetes.—The unfavourable effects of diabetes complicating pregnancy are manifested not by maternal mortality, which is fortunately very low, nor by grave progression of the diabetes, but rather by the frequent occurrence of accidents to the fetus; toxemia and eclampsia, coma and hypoglycemia. Our own conception of this problem is based upon an analysis of 271 pregnancies which have occurred in 191 diabetic women who

have consulted Dr. Joslin between 1898 and October, 1935. Essentially one-half of these cases occurred in the pre-insulin era, and one-half in the insulin era. A comparative analysis of these two periods shows surprisingly slight improvement of the insulin over the pre-insulin period. Thus, stillbirths have dropped from 29 to 25 per cent, and miscarriages and abortions from 22 to 16 per cent. We are, therefore, concerned with the investigation of the manner in which diabetes contributes to these failures and that form of treatment of the disease which most successfully avoids them.

Early abortion and miscarriage we attribute directly to the disease diabetes, for its incidence is three times more frequent among patients with hyperglycemia and glycosuria than it is among controlled cases. The characteristic pathology of uncontrolled diabetes gives us presumptive evidence of its harmful potentialities. The impregnated ovum implants itself in that portion of the uterus which has the richest supply of glycogen. Failure of the normal deposition of glycogen is the characteristic lesion of untreated diabetes. Lack of glycogen thus, theoretically, favours imperfect nidation.

Toxemia and eclampsia occur some 50 times more frequently in the diabetic than in the normal child-bearing population at large. This is most usual in the younger and consequently severer diabetics. Severity of disease rather than its control seems to favour the occurrence of this complication.

Stillbirth is a third, perhaps related, condition. For years the obstetrical diabetic literature has contained accounts of the frequency with which an overdeveloped, macerated fetus has been born to the diabetic mother. Here we wish to emphasize that this is not an unfailing characteristic of diabetes. The very fact that half of all these pregnancies ended successfully prior to the general use of insulin shows without further comment that this is not the case. The cause of this overdevelopment, characteristic of so many of these pregnancies, has never been quite clear. It is natural that it should be attributed to overnutrition secondary to the elevation of blood sugar, and blood fat, to the products of acidosis, or to hypoglycemia. Signs of these were lacking in our own series.

Although it is granted that all of these factors need further investigation, still a new and interesting clue appears in the work of

G. V. and O. W. Smith⁹ who have demonstrated that an excess of prolactin is characteristic of the toxemia of pregnancy, more recently of the toxemia of diabetic pregnancy, and toxemia we know occurs with great frequency in the diabetic, actually one out of every six of our own patients. Further, Snyder and Hoopes have demonstrated that injections of prolactin produce exactly the picture we see in diabetes, over-development, death, and maceration of giant rat and rabbit fetuses. Up to the present time G. V. and O. W. Smith have made complete analyses in only 9 of the cases of this series, and the special investigation has been under way for rather less than a year. In 3 of the 9 there was a definite increase of the serum prolactin. All three of these mothers were delivered of the giant type of fetus, whereas the remaining six with normal prolactin were not. Thus, we believe that two definite forward steps have been made; the first, when Dr. R. S. Titus decided to deliver these patients prematurely to anticipate the death of the fetus *in utero*. This was not entirely satisfactory, for we knew that not all of these patients were predestined to the development of this complication. We had no way of telling when it would and when it would not occur. The second, when G. V. and O. W. Smith seem to have given us a biological test which may indicate those very cases in which the fetus is of the giant type described as characteristic of diabetes.

Congenital defects,¹⁰ hypoglycemia and asphyxia complicate the neo-natal period. Congenital defects are doubtless beyond our therapeutic control. They are, we believe, related to a disease which is genetic in origin. It is an interesting corollation here to note that Dr. Richard Wagner has already reported the great frequency with which congenital anomalies occur in the true juvenile diabetic patient. Hypoglycemia may be a dangerous complication in the neo-natal period. It may result from a maternal overdose of insulin, or it may be due to an overproduction of fetal islet tissue.

Asphyxia of the child of a diabetic is a real problem and greatly to be feared if the patient has had normal labour, because there will be a tendency for prolonged labour due to the large size of so many of the babies. Further, insulin is capable of producing cerebral oedema. Perhaps most important of all is the

fact that the alkali reserve, measured by the plasma-combining power, is lower on the average in the diabetic than in the child of the non-diabetic. Thus, Eastman¹¹ has shown that in normal delivery the carbon dioxide content of the blood is 48; in difficult deliveries with anaesthesia it dropped to 40; and in asphyxia to 38. In our patients the plasma carbon dioxide combining power, not quite the same test that Eastman used but which gives a higher rather than a lower value, was distinctly low, for the average was 35 and the range from 19 to 52. Thus, asphyxia is a problem greatly to be feared.

The management of the diabetes during pregnancy varies with the problems of each trimester and with the individual case. Monthly, or even twice monthly, visits are necessary, not only by the obstetrician but also by the physician. The first trimester is concerned not only with the dietetic control of nausea and vomiting but with the readjustment of the diabetic regime, which necessitates the consideration of an accurate control of diabetes to prevent spontaneous abortion. If hourly feedings of carbohydrate foods are given in amounts up to 150 grams, or the administration of parenteral glucose, 5 per cent subcutaneously, or 10 per cent intravenously, are necessary, a new schedule for insulin must be adopted, and we plan to administer it according to emergency prescription. Test the urine every 2, 3, 4 or 6 hours, and give 20 units of insulin for a red test, 16 if the test is orange, 12 if yellow, and 6 if yellow-green. If nausea and vomiting are not complicating factors the first trimester does not require any particular change in the patient's regime. In the second trimester we are concerned mostly with the low renal threshold and the increased requirement for food. We believe that changes in insulin must be made upon blood sugar estimations only. In the early third trimester our chief concern is the possible development of acidosis. By this time the basal metabolic rate is elevated some 20 per cent. A caloric increase in the patient's diet is definitely necessary. The baby needs 50 grams of glucose daily, and allowance for this should be made in the mother's diet. Either the loss or the gain in tolerance for carbohydrate may be characteristic of this period, and we plan to give from 150 to 200 grams of carbohydrate, 1 gram of protein per

kilogram of actual weight, and 30 calories per kilogram of actual weight.

Labour increases the changes characteristic of the third trimester, namely, the elevated metabolism and depletion of glycogen. If normal labour is selected, then the patient will require first of all constant attendance, for she is a potential coma case, 150 to 300 grams of carbohydrate by mouth or parenterally, and insulin according to blood sugars and urinalysis as in the early part of pregnancy. If Cæsarean section is chosen there is essentially no danger of acidosis, but more of hypoglycæmia, and we therefore watch the blood sugar carefully, and prefer to maintain it between 150 and 200 milligrams. This patient is treated as any surgical case with urine specimens or blood sugars, if necessary, every 3 hours after operation, and insulin administered accordingly.

Failure of normal lactation is another characteristic of diabetic patients. This is possibly due to the lack of oestrin or the specific lack of the lactogenic hormone of the pituitary gland. The failure does not appear to be dependent upon diet, for it has occurred when patients have received 2,500 to 3,000 calories.

Infections and sepsis, contrary to expectations, have been exceptional.

Eugenic and genetic problems arise. Until the treatment of diabetes, even as good as it is today, is improved, we believe that diabetics should not have numerous pregnancies. Diabetes is a chronic, potentially incapacitating, disease, predisposing the patient, even in youth, to premature old age, manifested by arteriosclerosis, cataracts, retinal hæmorrhages, neuritis—all of which are recognized in the diabetic under 20 years. One must remember, as Dr. Joslin has so often pointed out, that the actual age is more nearly the chronological plus the duration of the diabetes. Perhaps, most important of all, we must ask what are the child's chances of inheriting diabetes, for we do believe there is evidence that the potentiality of developing diabetes is inherited; but it is inherited insidiously through a simple, Mendelian recessive gene, so that it is necessary for both parents to contribute the genes for diabetes. A diabetic may arise from two diabetics, from a diabetic and an hereditary carrier, or from two hereditary carriers. The incidence of hereditary carriers is, we estimate, 25 per cent in random matings. Thus,

the chances of a child of a diabetic becoming diabetic are one in four, but it must be remembered that all the children of diabetic patients are hereditary carriers of the disease.

PROGNOSIS

In any consideration of the juvenile or the young diabetic two questions are uppermost in our minds; is there any evidence of curability of diabetes, and what work is being done which may lead to eventual cure of the disease? A very small number, specifically 14, in a series of 1,063 cases of juvenile diabetes, appeared to have spontaneously arrested diabetes. These cases were treated in no fashion different from the average diabetic child. They are now aglycosuric, eating freely, not taking insulin, and some have passed insurance examinations and tolerance tests.

Permanent arrest of diabetes has been sought by the surgeon and by the physiologist. Thyroidectomy is not justifiable. Adrenalectomy and severing of the splanchnic sympathetic have increased the sensitivity to insulin somewhat. Ligation of the pancreas to produce hypertrophy has not been entirely successful. There has been some hope that quantities of pancreatropic hormone will be isolated. This in

the end will be a more physiological method of treatment for diabetes than insulin itself; but up to the present time, insulin and protamine insulin have been the great therapeutic advances. The change which protamine insulin may produce may be far-reaching indeed. Whether one adheres to the theory that the high blood sugar or the high blood fat is responsible for complications in diabetes the new preparation conquers both, and will give satisfaction because its value in these metabolic defects has been demonstrated. In all probability the severe diabetic, who in 1950 will have survived 15 years of the disease, may present a picture quite different from that of the long duration diabetic whom we presented today.

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AN UNUSUAL CASE OF MENINGOCOCCUS MENINGITIS*

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A PATIENT who was admitted to the Royal Victoria Hospital, Montreal, with remittent fever, proved to have meningococcus septicæmia and later developed meningitis. He exhibited clinical and bacteriological features of sufficient rarity and importance to warrant description.

CASE REPORT

(R.V.H. No. 68688), a male, aged 36, was admitted on September 21, 1934, complaining of recurrent daily chills and fever for seven weeks previously; poor appetite; and change in his voice for a like period. He had had pyrexia reaching 103°, with daily remissions, together with a rash.

Past history.—Gonorrhœa 18 years previously, with a reinfection 5 years ago. There was nothing otherwise significant except his association a short time before admission with a friend who was suffering from typhoid fever.

Physical examination.—On admission he seemed a fairly well-nourished man, though pale. With a furred

tongue, pyorrhœa, pharyngitis, and small red tonsils he had a profuse naso-pharyngeal discharge of tenacious, pearly-grey mucus, with yellowish flecks. There was a rash consisting of rather irregular, raised, reddish spots on the dorsum of the hands, arms, feet and legs, some of which were slightly pustular. Temperature, 100.2°; pulse, 92; respirations, 22. The red blood cells were 4,160,000 and the white blood cells, 15,000; hæmoglobin, 77 per cent. The neutrophils were increased, with a deviation towards immature forms. The sedimentation rate was increased.

Clinical course.—The patient's chills continued practically every day, after which his temperature rose to 103 or 104°, remained there three or four hours, and then rapidly fell to normal, where it would stay until next day. Thus a clinical picture presented which was too indefinite to allow of a diagnosis without further investigation.

September 22nd.—The Wassermann test was negative; agglutination tests against *B. typhosus*, *B. paratyphosus A* and *B* were negative. Aerobic and anaerobic blood cultures were negative. September 25th. A special oto-laryngological examination showed only the existence of a paralysis of the left laryngeal nerve. A blood count did not add anything new. September 27th.—Agglutination tests against the *Brucella* group were negative in a range of dilutions from 1:20 to

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1:2,560. September 28th.—Oto-laryngological examination confirmed the previous finding. The blood was examined for evidence of rat-bite fever (by animal inoculation) and for malaria (by stained blood films). Neither was discovered. October 1st.—The patient's urine was examined by animal inoculation for evidence of Weil's disease, with a negative result.

The right testicle was painful and enlarged and the epididymis was swollen and tender; the left testicle appeared to be normal. The patient was given a therapeutic test dose of 0.3 g. of novarsenbenzol intravenously, which was followed by a cessation of the chills for 48 hours. October 2nd.—The direct and indirect van den Bergh tests were negative. October 3rd.—Lumbar puncture revealed nothing abnormal. The Wassermann test on the cerebrospinal fluid was negative; the blood Wassermann was negative; the gonococcal complement fixation test was doubtfully positive.

October 5th.—The gonococcal complement fixation test was repeated, with the same result. Blood cultures, using special media, were negative. October 6th.—A second injection of novarsenbenzol (0.3 g.) was given without result. October 8th.—Three large, irregular, raised, red spots appeared—one on each forearm and one on the left thigh. October 9th.—Laryngoscopic examination showed paralysis of the left recurrent laryngeal nerve. The Kahn test on the blood was doubtful. October 17th.—Blood cultures yielded a small number of Gram-negative cocci of the *Neisseria* group, which fermented maltose but not glucose, and grew at 37° C. but not at room temperature. One strain (No. 237) was isolated for further study.

patient was discharged, at his own request. He had not had chills for five days. On arriving home he remained in bed until the next day. Then, after returning from a short walk, he was seized with a terrific headache. This persisted throughout the next day, and was associated with some vomiting and pain in the back, legs and arms.

November 16th.—Readmitted to hospital (R.V.H. No. 69143) with a temperature of 101.6° F.; pulse, 105; respirations, 24. There was slight stiffness of the neck. There were no other abnormal findings, on ordinary examination. Forty c.c. of cerebrospinal fluid were withdrawn; the initial pressure was 160 mm. and the final pressure 100 mm. The fluid was cloudy and gave a positive Pandy test. It contained 220 cells per c.mm., 90 per cent of which were polymorphonuclears. No organisms were found, either on films or by culture.

During the last few days of the patient's first admission further tests had been carried out to identify the organisms obtained. The blood cultures, as already noted, gave atypical cultural characters, yet such as are sometimes given by the *Meningococcus*. The organism obtained from the naso-pharynx presented the cultural characters usually accepted for the *Meningococcus*. Heat-killed suspensions of 100 million bacteria per c.c. were made up from the four isolated strains (Nos. 237, 393, 400¹ and 400²) mentioned above, and from three types of meningococci (Gordon and Murray) available at the Bacteriological Laboratory. These suspensions were put up with serial dilutions of a well known firm's (A) antimeningococcus serum. The results are given in Table I.

The above procedure was repeated, using the product

TABLE I
DILUTIONS OF SERUM OF FIRM A IN NORMAL SALINE

Organism	200	400	800	1600	3200	6400	Control
Type I.....	± to D	(+)	(+)	0	0	0	0
Type II.....	+++	+++	+++	(+)	(+)	0	0
Type III.....	+++	+++	+++	++	0	0	0
237.....	D	0	0	0	0	0	0
393.....	(+) to D	0	0	0	0	0	0
400 ¹	D	0	0	0	0	0	0
400 ²	(+) to D	0	0	0	0	0	0

D means denser than control; (+), a trace of agglutination.

October 20th.—Cultures from the urine gave only *Staph. pyogenes aureus*. October 22nd.—Gonococcal complement fixation tests on the patient's blood were negative. October 25th.—A flat plate of the thorax showed only some thickening at each hilus. October 26th.—The prostatic secretion was negative for gonococci, microscopically. On culture heavy growths of staphylococcus, several varieties of micrococci, and non-haemolytic streptococci were obtained. Members of the *Neisseria* group were not found. October 30th.—X-ray examination of the accessory air sinuses revealed no disease. October 31st.—Bladder urine was cultured and *Staph. pyogenes* and *Staph. epidermidis* only were found.

November 5th.—The gonococcal complement fixation test on the blood was not definitely positive. Blood cultures again yielded *Neisseria* of the type obtained on October 17th. This strain was kept for further study (No. 393). Cultures from the naso-pharynx yielded small numbers of *S. viridans* and *S. haemolyticus*, with a rich growth of *Neisseria* which fermented both glucose and maltose and grew on ascitic agar but not on plain agar. The primary cultures in this case were made at the bedside from the naso-pharyngeal secretion which was immediately smeared on warm blood-agar plates. Two strains here were isolated for further examination (Nos. 400¹ and 400²).

November 9th.—The electrocardiogram was normal. November 13th.—Blood culture gave again a *Neisseria* of the same character as before. November 14th.—The

of a second firm (B), with the results shown in Table II.

These suspensions were then put up against serial dilutions of the patient's own serum, of from 1:10 to 1:1,280. None of the strains was agglutinated.

November 17th.—Intrathecal serum treatment was started. Because of its higher agglutination power on the patient's strain the product of firm B was used almost entirely for treatment. It was given also intravenously. The cerebrospinal fluid showed many intracellular *Neisseria* in smears which were found on culture to have the same characters as those previously isolated from the blood (i.e., fermenting maltose but not glucose). The initial pressure of the fluid, on puncture, was 270 mm. Twenty-five c.c. of cerebrospinal fluid were withdrawn and replaced by the same amount of serum. This caused severe pain down both legs and in the lumbar region. On the evening of this day 50 c.c. of serum were given intravenously. November 18th.—At 9.30 a.m. 60 c.c. of serum were given intravenously, again being followed by much pain. November 19th.—At 1 a.m. 60 c.c. of serum were administered intravenously. At 3 a.m. lumbar puncture was done. The initial pressure was 450 mm. Twenty c.c. of turbid fluid were withdrawn and 15 c.c. of serum were given intrathecally; again, much pain. The cerebrospinal fluid showed many polymorphonuclear leucocytes, a few monocytes, and a few Gram-negative intracellular bodies (? microorganisms). No growth was obtained on culture. At 5.30 p.m. 15 c.c. of cerebrospinal fluid were withdrawn and replaced

TABLE II
DILUTIONS OF SERUM OF FIRM B IN NORMAL SALINE

Organism	200	400	800	1600	3200	6400	12800	25600	Control
Type I.....	++	++	++	(+)	0	0	0	0	0
Type II.....	+++	+++	+++	++	(+)	+	0	0	0
Type III.....	+++	+++	+++	+++	++	+	(+)	0	0
237.....	++	+	+	0	0	0	0	0	0
393.....	+	(+)	0	0	0	0	0	0	0
400 ¹	+	0	0	0	0	0	0	0	0
400 ²	++	0	0	0	0	0	0	0	0

by 10 c.c. of serum. This caused a great deal of pain, despite the fact that morphine and hyoscine had been given previously.

November 20th.—At 6.30 p.m. 40 c.c. of cerebrospinal fluid were withdrawn and 20 c.c. of serum given. No organisms were seen and culture was negative. About this time the patient suddenly showed signs of much improvement. His temperature, which had been running between 100 and 102° F., within two hours fell to 98°, and his pulse, from 124 to 104. Next day, his cerebrospinal fluid showed no organisms on smear and no growth was obtained, but his blood culture was still positive. In the afternoon his temperature rose to 99.6°, fell again, rose to 100° the next day, and then dropped to normal, where it remained. Smears and cultures of the cerebrospinal fluid, withdrawn each day, showed no organisms. The number of the contained cells gradually decreased, the polymorphonuclears more rapidly than the others. The blood culture taken on November 25th was

largely as differentiation was made between the agglutinations of type I and type III. Precipitation tests were carried out on some of the cerebrospinal fluid collected for culture. The fluid was centrifuged and the clear supernatant fluid, in serial dilutions (1, 1/2, 1/3, and so on up to 1/32), was put up against antimeningococcus serum in dilutions of 1/5 and 1/20. Precipitation of the antibody was much more marked with the serum produced by Firm A than with that of Firm B.

December 8th.—The patient had a slight recurrence of his troubles. His temperature rose to 100° and his pulse to 110. Associated were headache, stiffness of the neck, and a positive Kernig sign. Lumbar puncture was done immediately. An increased cell count (1,300 per c.mm.) was found, and a positive Pandy test. On smear most of the cells were found to be polymorphonuclears. No organisms were found on smears or culture. Blood culture was also negative. The patient was immediately desensitized and 30 c.c. of antimeningococcus serum (B)

TABLE III
DILUTION OF SERUM (B) IN NORMAL SALINE

Organism	200	400	800	1600	3200	6400	Control
Against Adsorbed Serum (B):							
Type I.....	+	(+)	0	0	0	0	0
Type II.....	++	++	++	+	0	0	0
Type III.....	+++	+++	+++	++	(+)	0	0
Against Serum (B) before Adsorption:							
Type I.....	+++	++	+	(+)	0	0	0
Type II.....	+++	+++	+++	+	(+)	0	0
Type III.....	+++	+++	+++	++	(+)	0	0

negative. From this date the patient improved markedly. Cultures from his blood and cerebrospinal fluid remained negative, but his naso-pharynx still gave cultures of *Meningococci*. The temperature and pulse remained normal and the patient felt remarkably well.

Attempts were made to type the causative organism according to the classification of Gordon and Murray. Monovalent type sera were not available, so the test devised by Fildes and Baker¹ with polyvalent serum was used. Four c.c. of a suspension of 4,000 million per c.c. of strain No. 237, isolated from the patient's blood, were mixed with 40 c.c. of a 1:50 dilution of antimeningococcus serum (B), incubated for 20 hours at 37° C., and then centrifuged. The supernatant fluid was diluted in series and put up against a 1,000 million suspension of the three available type cultures and compared with the agglutination of these cultures by the serum before adsorption. The results are given in Table III.

Accordingly, it would appear quite justifiable to assume that the patient's organism belongs to type I since the agglutinations of type I were markedly adsorbed, while those of types II and III remained unaltered, particu-

larly as differentiation was made between the agglutinations of type I and type III. Precipitation tests were carried out on some of the cerebrospinal fluid collected for culture. The fluid was centrifuged and the clear supernatant fluid, in serial dilutions (1, 1/2, 1/3, and so on up to 1/32), was put up against antimeningococcus serum in dilutions of 1/5 and 1/20. Precipitation of the antibody was much more marked with the serum produced by Firm A than with that of Firm B.

December 14th.—A modified Solis-Cohen test² was carried out, in an attempt to determine the bactericidal power of the patient's blood. A twelve-hour growth of meningococci, isolated from his blood on December 12th, was taken, and a suspension of 4,000 million in glucose broth containing 5 per cent human serum was made up. One-tenth of a c.c. of this was put in test tube No. 1; 0.1 c.c., diluted ten times, was placed in test tube No. 2. Thus serial dilutions were made. Two such series of tubes were set up, one for the patient and one on a control, for which a comparatively well convalescent patient was chosen. One c.c. of blood, freshly drawn from the patient, was put in each tube of one series, while the same amount from the control patient was put in each tube of the second series. The mixtures in both series were allowed to clot and were incubated for twenty-four

hours at 37° C. Next day the clot in each tube was broken up and cultured for growth, with the following results (Table IV).

TABLE IV

Dilutions of Culture	4000 x 10 ⁶	400 x 10 ⁶	40 x 10 ⁶	4 x 10 ⁶	0
Patient	growth	0	0	0	0
Control	growth	growth	0	0	0

This means that 1 c.c. of the patient's blood, eight days after the last dose of serum, killed the meningococcus in concentrations between 400 and 4,000 million cocci per c.c., while the control blood would do so only between 40 and 400 million. This test was repeated on December 17th with the same result.

As the cultures from the naso-pharynx remained positive it was desirable to free his nose from meningococci. Abnormalities of the naso-pharynx were searched for, but none were found. Nasal douching with physiological saline, followed by peroxide of hydrogen, was carried out four or five times a day. This treatment has been found effective by many workers (Dubois and Warren, Sophian,⁷ Bethege, and others). Between times inhalations of oil of eucalyptus were given, because Dopter³ has found that this is the most effective disinfectant among the essential oils. Also, argyrol, 10 per cent, was dropped into the nostrils twice daily. Periodic nasopharyngeal cultures were made and the number of meningococci was found to decrease gradually. Finally, on January 4, 1935, none could be found and, likewise, on January 9th. Treatment was stopped for forty-eight hours before each culture was taken. The patient was then discharged. He returned to the Out-door Department in March of the same year and *Meningococcus* was again found on culture from his naso-pharynx. A few months later his daughter was admitted to the hospital with a severe sore throat and *Meningococcus* was isolated from nasopharyngeal swabs.

COMMENTS

This case presents unusual features. Prolonged illness with septicæmia followed by meningitis, which was correctly diagnosed only after numerous and searching tests, has been described before, though rarely. Septicæmia (as indicated by positive blood cultures) and meningitis usually occur together, and, as Dopter remarks, it is difficult to decide which precedes the other. Murray⁴ believes, however, that the septicæmia always comes first. A number of cases like ours, with intermittent fever, septicæmia and late meningitis, described in the literature, cited by Dopter (*loc. cit.*), and a case mentioned by Zinsser and Bain Jones, in their text-book support the view that infection of the blood stream always precedes meningitis. That in our case positive blood cultures were difficult to obtain early in the disease, except when taken during a chill, while later they could be obtained even when there was no pyrexia (as in the case of the blood culture taken on November 8th), tends to show that the recurrent chills were due

to the periodic entrance of bacteria from the naso-pharynx (which was continuously infected) into the blood stream.

When meningitis did ensue it seemed to be precipitated by unaccustomed effort, as on rising prematurely from a sick bed, while the blood cultures and those from the naso-pharynx were still positive. Dopter states that such cases usually carry a high mortality, possibly because the diagnosis is not made soon enough to be a guide to treatment. Fortunately in our case serum therapy could be instituted almost immediately, in fact, as soon as the *Meningococcus* was found in the cerebrospinal fluid, because of the previous recognition of the septicæmia.

The strain of meningococcus isolated in this case was remarkable in that it fermented maltose and not glucose. Typically, both sugars should be fermented, although either one may be fermented before the other. Forms which ferment maltose only are very rare indeed.^{3, 6, 7} This unusual behaviour added confusion to the investigation of the case, particularly since there was a history of two attacks of gonorrhœa. The suspicion that there was a gonococcal septicæmia was made all the stronger because of the occurrence of epididymitis and an ever-increasingly positive gonococcus complement fixation test. The checking of the media and the occurrence of culturally typical meningococci in the naso-pharynx, together with the agglutination reactions, however, made the diagnosis of meningococcal septicæmia certain. Precipitation tests on the cerebrospinal fluid gave additional confirmation. Epididymitis and a macular eruption are, according to Dopter, not uncommon complications of meningococcal infection, though he gives no figures as to their frequency. The positive complement fixation test with gonococcus was to be expected.

After the second meningeal involvement attempts were made to determine the patient's ability to kill out the causative organism, using a modification of the Solis-Cohen test as devised by Heist.² This test showed that the patient's blood had a greater bactericidal power than that of the control patient. In the first test this immunity reaction might quite possibly have been due to the serum injections, but it is possible that the second test indicated that some active immunity had developed, particularly as the patient's disease did not recur after his passive immunity must have passed off.

Bloch and Hebert emphasize the necessity of administering the specific serum intravenously as well as intrathecally, even though Netter has shown that antibodies reach the blood when the serum has been given by the spinal route. This treatment certainly seemed to be successful in the case here described. Some importance, too, may perhaps be attached to the fact that the serum used was selected on the basis of the agglutination reaction of the patient's strain.

Finally, it would seem necessary, under the conditions exhibited by the case in the early stages, to attempt to control the nasopharyngeal infection. The method used seems to have been

adequate, although the argyrol may have been superfluous.

My thanks are due to Prof. J. C. Meakins for permission to publish the clinical notes, and to Prof. E. G. D. Murray for his aid in directing the investigation of this case.

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SOME PROBLEMS OF HEART DISEASE IN CHILDHOOD*

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THE problems that occur in children with heart disease pertain chiefly to diagnosis, prevention, and treatment. As the etiological factor is a rheumatic infection in the majority of cases (see Chart I), the problems that arise are involved with the occurrence of rheumatism in childhood. Other infections and congenital heart disease are responsible for a smaller percentage of cases of heart disease in children.

CHART I

CAUSES OF CARDITIS ADMITTED TO HOSPITAL FOR SICK CHILDREN DURING 1930-1931

	Cases
1. As a result of acute rheumatic fever in Hospital for Sick Children	60
2. As a result of previous acute rheumatic fever .	60
3. As a result of chorea in Hospital for Sick Children	51
4. Cause unknown, but diseased tonsils present ...	16
5. As a result of congenital heart disease	64
6. As a result of other infections, such as scarlet fever, diphtheria, influenza, septicaemia	18
Total number of cases	269

Rheumatic heart disease is fairly prevalent in children over three years of age. In the year 1930 there was a total admission into the Hospital for Sick Children of 6,970 patients, of whom 1.7 per cent had rheumatic heart disease. The above figures may not appear formidable, but

the seriousness of the condition lies in the possibility that further re-infection of the myocardium might occur, which may possibly result in premature death or in curtailing the activity of that child for life. The mortality rate of the years 1930-1931 was 10.9 per cent. The problem of rheumatic heart disease exists in all classes of people, but is found more frequently amongst those living in the poorer section of the city where the hygienic surroundings and living conditions are below standard. Another factor to be considered is the rheumatic family. In 24 per cent of the cases of rheumatic disease admitted into this hospital there was a history of rheumatism or carditis in one or more members of the same family. It is not known whether this is a familial susceptibility or a spreading of infection from contact.

It is contended by some observers that 100 per cent of children with rheumatic infection have cardiac involvement. Seham *et al.*¹ in their study of rheumatic heart disease in children found that acute rheumatic fever alone was responsible for 39 per cent of the cases of heart disease, but in combination with all of the other forms of rheumatic infection it is present in 83 per cent of all cases. In the year 1930, of those admitted into the Hospital with acute rheumatic fever and chorea 68 per cent developed carditis.

When the rheumatic infection is present in its most serious form, that is heart disease, there is

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no difficulty in diagnosing the condition. The problem that arises in diagnosis pertains to the milder types of heart involvement in which there is present a systolic murmur and no definite history of joint involvement. In this type of case various factors will have to be taken into consideration, such as the presence of frequent upper respiratory tract infection, tachycardia, if it is persistent, the presence of a low grade fever, and signs of general debility, such as pallor, loss of appetite, fatigue, and loss of weight. It has been reported that from 8 to 20 per cent of children have a functional heart murmur at one time or another, and to differentiate between a functional and an organic murmur is not always a simple matter. At the present time no satisfactory clinical differentiation is known. It has been stated that a soft systolic murmur with its point of maximum intensity at the base or internal to the apex is functional. But this alone is not sufficient evidence unless the general health and previous illness of the child are taken into consideration. It is found in many cases that a systolic murmur with its point of maximum intensity at the apex is organic in origin, but in the early cases of rheumatism there are exceptions to the rule. During this period the murmur may be inconstant, that is, it is heard at one time and absent the next. Sometimes it is merely a roughening of the first sound. A certain percentage of these children as time goes on will develop definite evidence of organic heart disease. In these cases the electrocardiogram and x-ray examination of the heart may be of help. It is important to decide whether a murmur is organic or functional, as the diagnosis of an organic murmur where a functional one is present has resulted in a normal child living a restricted life. These restrictions have been the basis for the development of behaviour problems. At times a diastolic murmur is heard during the course of an acute rheumatic infection and disappears as the infection clears up. This murmur is not due to a stenosis of the mitral valves, as the murmur of a stenosis takes several years to develop and as a rule after repeated re-infections of the myocardium.

There is the problem of the so-called "heart attacks" in children, which usually consist of fainting, weak spells, or præcordial pain. In the attacks of weakness and fainting one will have to differentiate between paroxysmal tachycardia,

the presence of the minor degrees of the convulsive state and the child with an unstable nervous system. An electrocardiogram will aid in the diagnosis of paroxysmal tachycardia, if taken during the attack. As a rule luminal prevents the attacks in the convulsive state, and inquiries into the living habits and environment of a child will aid in the diagnosis of the child with the unstable nervous system. Præcordial pain may be rheumatic in origin especially if there has been a previous or present history of rheumatism, while at other times it occurs in children with an unstable nervous system. In the latter cases there is smooth muscle spasm as a result of environmental tension or emotional unpleasantness.

The incidence of congenital heart disease in children is next in frequency to rheumatic heart disease. During the years 1930-31-32 there were 85 cases of congenital heart disease admitted into the Hospital for Sick Children. The seriousness of the condition lies in the high mortality rate during the first year. There were 57 cases of congenital heart disease under one year of age, and 11 at one year of age. The death rate in the group under one year of age was 57 per cent. Of these, 18 died under one year of age with bronchopneumonia. Clubbing is infrequently seen but cyanosis was present in 52 per cent of the cases. In infants the cyanosis may only be apparent on effort, and a mother will give a history of her child having blue spells. Congenital heart disease is diagnosed on the finding of enlargement of the heart and the presence of a systolic murmur with its point of maximum intensity in the first, second, third, or fourth interspace close to the left border of the sternum. In children under three years of age there may be a possibility of confusing this with a functional murmur, and over three years of age it may have to be differentiated from an organic murmur, particularly where there has been a previous history of rheumatic disease. Thrills occur more frequently with murmurs congenital in origin than they do with those organic in nature.

Congenital heart disease may not be diagnosed during life or in early infancy. In 10 cases in which a ductus arteriosus, patent inter-ventricular septum, or malformation of the aortic valve was found post mortem, no murmur was heard in hospital. It is not always possible to diagnose congenital heart disease in infancy. Cases are

on record of children having no heart murmur in early infancy, but sometimes after the sixth month the murmur has appeared. In one case at the hospital it was not apparent until the child was examined at 5 years of age, though it had been examined on two other occasions. If there is any difficulty in diagnosing congenital heart disease x-ray examination and electrocardiograms are often useful.

The treatment of heart disease in children is first directed towards its prevention, and, if infection has occurred, the prevention of further reinfection of the myocardium. This is not always possible.

In the ambulatory cases it is important to maintain the optimum health and to prevent the occurrence of upper respiratory tract infection. Improper diet, poor housing, improper hygienic care, and northern climates affect the health of the child. This child should dress warmly, live in the suburbs or dryer section of the city, have 11 to 12 hours rest each night, and be given a good nourishing diet. It is allowed to live a normal life with no entailment in activity even though a systolic murmur be present, providing no other manifestations of rheumatic infection are present. If tiredness is complained of extra rest is advised, even to the extent of taking the child out of school for a while. On the appearance of anæmia, iron medication is prescribed. Uncomplicated upper respiratory tract infection is treated in the ordinary way, but if accompanied by joint pains rest in bed and salicylate therapy are ordered. The treatment of intermittent growing pains depends upon their frequency. If their occurrence is infrequent salicylates are given, but, if frequent, rest in bed is needed as well.

The prevention of upper respiratory tract infections is to be stressed. In the 96 cases of acute rheumatic fever there was a preceding acute upper respiratory tract infection in 33 per cent of the cases, which occurred 10 to 19 days before the arthritis. Of the cases admitted with rheumatic carditis there was a preceding upper respiratory tract infection in 30 per cent. An important factor in the prevention of upper respiratory tract infection is the removal of tonsils and adenoids. This does not always prevent the occurrence of upper respiratory tract infection, but in the majority of children the infections are decreased in number and are not so severe as formerly. Kaiser² has found that

removal of the tonsils and adenoids for the common cold resulted as follows. In 8 per cent the severity and number of colds were not reduced at the end of one year, in 7 per cent at the end of 3 years, and in 22 per cent at the end of 10 years. In a similar control group the incidence and severity of colds was just the same during the one- and three-year period of observation, but at the end of 10 years only 31 per cent were not relieved. In this survey he found that rheumatic infection developed in 2 to 3 per cent of children in which tonsillectomy and adenectomy had been performed and in 3 to 5 per cent of children in which the tonsils had been left in. Growing pains occurred in 7 to 8 per cent with tonsils out and in 9 per cent with tonsils present. He concluded that removal of the tonsils offered the child a 33 per cent better chance of not developing rheumatic infection than if they were left in. In the group studied at the hospital the tonsils were present in 82 per cent of the cases of acute rheumatic fever and in 74 per cent of the cases of rheumatic carditis. There was a recurrence of rheumatic carditis in 11 per cent after the tonsils and adenoids had been removed.

Tonsils may safely be removed three weeks after an acute upper respiratory tract infection, providing no infection of the myocardium has taken place and the temperature is normal. In hospital practice tonsils and adenoids were removed four to six weeks after an attack of acute rheumatic fever, and in cases where there has been moderately severe infection of the myocardium at least two weeks are allowed to elapse after the temperature has become normal and the pulse is slow and steady.

Unfortunately a certain percentage of children will under careful treatment and close supervision have repeated recurrences of their rheumatic infection, but even more discouraging is the treatment of rheumatic heart disease, especially in those children with repeated exacerbations of myocarditis as occurred in 13 per cent of the group studied. In this type of case the more serious manifestations of heart disease are found, such as cardiac decompensation, pericarditis, fibrillation and heart block, though the two last mentioned are seldom seen, there being two cases of each during the 1930 and 1931 period. Stroud³ found in his survey of 307 children who had rheumatic heart disease that 40 per cent were either hopelessly disabled or dead at the end of a ten-year period.

The treatment of rheumatic carditis consists of prolonged rest in bed and administration of salicylates. The child is allowed up, even though a murmur is present, when all signs of myocardial infection has disappeared, such as fever, tachycardia and swinging pulse, on condition that the child appears and reacts like a healthy child and the exercise tolerance is normal. On the first day he is allowed up five minutes and on each succeeding day an additional five minutes until he is up for one hour daily. During the second hour, fifteen minutes is added each day. A period of 4 to 12 weeks in bed is usually necessary in the mild and moderately severe cases, while in the severe cases

a much longer period is allowed. For many weeks after, a rest is required in the afternoon. School is allowed for half a day at first, but with no strenuous exercise or competitive games. Children with badly damaged hearts should receive extra-mural teaching, which can be readily obtained in the larger cities. This removes the child from the temptation of entering games beyond his capacity and also lessens his chances of upper respiratory tract infection.

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ALCOHOL AND GLYCERINE IN THE TREATMENT OF PYOGENIC INFECTIONS

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A PAPER by L. H. McKim,¹ of Montreal, at the Clinical Congress of Surgeons in 1927 drew my attention to the use of alcohol in dehydrating the tissues in hand infections. I immediately put the idea into practice, particularly in infections of the tendon sheaths. Its value was soon very evident. It was observed that the greater the opportunity for dehydration, the better the result. McKim advised the use of liquid paraffin with bismuth and iodoform in the dressing following dehydration with alcohol. Iodoform I had long since given up on account of its disagreeable odour, and because it becomes, with bismuth, a foreign body. We frequently see this in x-ray pictures of war wounds which had been treated by the then popular B.I.P.P. Liquid paraffin did not appear to quite fit into the picture as it certainly would not dehydrate. To clear the air and make this presentation more simple I take the liberty of quoting verbatim from McKim's paper:—

The Technique of the Incision.—General anaesthesia is preferable. In whitlow and paronychia local anaesthesia (lateral nerve block with novocaine) may be used, but even in these cases better results are obtained with general anaesthesia. Ethyl chloride should never be used.

The operation should have a bloodless field. This is most important. If a tourniquet is not used, many small pockets of pus will be missed: this is especially true in early whitlow. The tourniquet should be removed and any gross hæmorrhage controlled before the final dehydration.

The incision should be a correct and adequate one. It is wise to complete the incision feeling that it has been

made a little too big. All partitions in the cavity should be broken down and all necrotic material removed, using a few layers of gauze over the end of the finger as a curette. Be sure that the wound is completely explored. The cavity should be dehydrated with alcohol, (rubbing alcohol or methylated spirits). The cavity should be packed tightly with sterile gauze soaked in liquid paraffin to which a small quantity of B.I.P.P. has been added. A plain dry sterile gauze dressing should be applied and secured by a bandage and the hand put at rest in the position of function. Splints are applied loosely as a means of securing rest rather than fixation.

From this point I started, except as mentioned above, bismuth and iodoform were omitted. As in a dehydrating process liquid paraffin seemed to have no place, a suitable substitute with dehydrating power was sought. Continued soaking in alcohol would produce dehydration but would require frequent applications, cause irritation, and the dressing would stick to the wound. Calcium chloride certainly dehydrates but also cauterizes the tissues. I would, however, suggest that it is quite probable calcium chloride has a real place in the dehydrating treatment of infections. It is too early in the experimental stage to come to any conclusion. Glycerine seemed to be the logical agency through which to continue the dehydration, lessen the possibility of the dressing adhering to the tissues, and keep the wound free from contamination. After trying various percentages of glycerine from 100 per cent down, the diluent being rubbing alcohol (Ontario formula), a combination of equal parts

of glycerine and rubbing alcohol has been found the most satisfactory for general use.

In considering such a mixture it is evident that the alcohol would evaporate fairly quickly, leaving pure glycerine. Some simple way of replacing the lost alcohol is required. It is essential that the sterile dressing be not removed. The alcohol could be poured on the outside of the dressing and allowed to soak in through the lower layers, but the outside of any dressing soon is dirty. This seemed a genuine obstacle to such a procedure. However, alcohol so applied was tried through the most filthy and infected bandages. Nothing amiss came of it. Apparently the alcohol kept itself sterile as it advanced through the dressing. Certainly it did not appear to carry any fresh infection into the wound.

Besides replacing the evaporated alcohol, it has been found expedient to renew the glycerine more frequently than it was indicated to change the dressing, that is, a dressing should not be tampered with any oftener than is absolutely necessary. For example, in an incised, infected, tendon sheath, packed with gauze soaked with 50 per cent glycerine and alcohol, five or six days should elapse before this packing is removed. In many cases it is expedient and beneficial to leave it longer. On the other hand, the glycerine should be renewed every six to eight hours. This is necessitated by its hygroscopic action, which loads it with water and so spoils its function.

When a satisfactory routine for infected tendon sheaths of the hand was obtained this glycerine and alcohol treatment was tried on all types of tissue infections. I shall not attempt to enumerate them, but at the end of this paper will give examples from a series of cases treated in the out-patient department of the Ottawa Civic Hospital which will be sufficient illustration of its scope. There is no type of pyogenic tissue infection in which it appears to be ineffective and in most its effects are to be preferred to commonly used methods.

Dehydration, as a treatment of pyogenic infections generally, appealed to me. I could never satisfy myself that the application of any antiseptic to the surface of infected tissue, even after multiple incisions, was of much value. Certainly an agent so applied would not get far into the depths of the infected tissue. What did penetrate would be greatly diluted by the body fluids and so rendered well-nigh useless. In addition,

the aqueous vehicle of the antiseptic undoubtedly soaked into at least the surface layers of the tissues. This could but be harmful, as it increased the already too great turgidity of the infected tissues. With infection there is inflammation, a pouring out of aqueous lymph into the tissues, an increase in intra-tissue pressure, a consequent slowing of circulation, a lessening of blood supply, a lowering of tissue vitality and consequent diminution of resistance to infection. Watery applications increase this turgidity. True, they may dilute the toxins a bit and wash the surface.

In contrast a dehydrating agent causes a flow of lymph to the surface carrying with it toxic products of infection as well as the bacteria. It reduces the tissue swelling and intra-tissue pressure, thus allowing a greater blood supply. There is an increase in the determination of the system's antibodies to the infected part, thus assisting nature to overcome the infection. Glycerine and alcohol, besides being hygroscopic in action, are definitely antibacterial and so the bacteria discharged into the dressing become the prey to this action.

The production of bacteriophage seems to be assisted by glycerine and alcohol. I say "seems", for there is, at present, no way to prove or refute such a statement. The remarkable manner in which infections clear is satisfactorily explained through such a supposed beneficial action of this mixture. For the practical application of this idea I have endeavoured to evolve a safe, simple and fool-proof technique, as effective in the office practice of the general practitioner as in the wards of the most up-to-date hospitals.

The general method of application of this treatment is as follows: In surface infections where the skin and subcutaneous tissues only are involved:—

1. Avoid incision until pus is localized and circumscribed.

2. Cleanse the area with alcohol. Carbon tetrachloride is also most useful in removing "salves" and the remains of adhesive plaster.

3. A few layers of sterile gauze (in office practice clean gauze removed from a commercial package) of sufficient size to completely cover all the oedematous area are soaked in glycerine and rubbing alcohol, equal parts, and laid on the affected area. This is covered with a thin layer of absorbent cotton and lightly bandaged with an open-woven gauze bandage. An additional

amount of glycerine and alcohol may then be poured over the area at once. No waterproof covering is used.

4. In the case of a limb, it should be splinted or rested; if hand or arm, should be carried in a sling.

5. The patient is given prescriptions for lotion No. 1, which is glycerine and alcohol equal parts, and for lotion No. 2, which is straight rubbing alcohol. Instructions are given to apply a small amount of lotion No. 2 every two to three hours, or more frequently in hot weather when evaporation is more rapid. The amount will vary with the size of the dressing: a half teaspoonful is enough for a finger. A similar quantity of lotion No. 1 is to be applied every six to eight hours, at which time lotion No. 2 is omitted. The quantities of these two lotions required will of course vary with the size of the dressing. A common amount to prescribe is six ounces of No. 1 and eight ounces of No. 2.

6. The whole dressing is removed and replaced every twenty four hours, early in the treatment, although an interval of two to three days may elapse without any particular loss to the effectiveness of the treatment.

7. Careful instructions are given that the dressing must not be removed to make the above applications and that no water be applied to the dressing. Should the dressing become moistened with water, as frequently happens in hands, a larger quantity of No. 2 lotion should be immediately poured over the dressing.

In deeper infections the usual teaching as to incision applies. When the incision has been made the abscess cavity or tendon sheath should be thoroughly dehydrated with rubbing alcohol and packed firmly with gauze soaked with alcohol and glycerine. Should the cavity be large or deep it is well to incorporate in this packing a small rubber tube through which further applications of glycerine and alcohol may be made.

One inclines to delay in making an incision; frequently this may be avoided entirely.

Subsequent treatment is the same as outlined above, except that where the tube is inserted the lotions are applied through the tube instead of on the dressing, and the packing is left in place five or six days or even longer. Experience will soon teach how long the packing may be left; one can almost say the longer, the better, and I recall one patient with a broken-down axillary gland who returned for a second dressing in

thirteen days, with very satisfactory results. Where there is a sinus or inverted, deep cavity all that is necessary is to inject the glycerine and alcohol therein at regular intervals. The interval will vary with the degree of infection and swelling within the tissues. Every three to six or even eight hours.

When the dressings are being changed scrupulous care must be taken not to squeeze the inflamed area. This is most important and cannot be too strongly emphasized. There is no small amount of satisfaction in pressing firmly into a purulent area and producing large "gobs" of thick pus. It impresses the surgeon as well as the patient, but we must refrain from such a procedure and forego the pleasure. The only interference that should be considered is gently wiping the skin about the area with a soft bit of absorbent cotton in a sterile forcep. It is well to dip this cotton in rubbing alcohol. In addition one *may* be permitted to gently pick off any *free* sloughs. That is if they are free. This is not necessary, really, for if they are free they will come away themselves and should they be not free they should not be touched.

In some very sensitive tissues, or with those hypersensitive persons who cannot seem to tolerate even the least discomfort, it is found necessary to lessen the percentage of alcohol. Pure glycerine can be used with good results, and when one is doubtful about the toleration it is well to begin with this and slowly add alcohol. One dram of alcohol to the ounce is even better on the start and perfectly safe.

While the cases quoted are ambulatory ones the procedure is none the less applicable to bed patients, whether they be at home or in hospital. This is a report as from the out-patient department of a city hospital. This method is of equal value in such conditions as acute and chronic osteomyelitis, appendiceal abscess, and gangrenous appendicitis with an indurated cæcum, acute mastitis, acute pyogenic arthritis, etc.

The following will illustrate the scope and value of the suggested method. The routine as above was carried out and proper instructions given. Of what was done at home there was neither control or report, as is usual with such patients in private practice. Any departure from routine is mentioned. Dressings were changed, at most, 3 times a week, except as noted.

CASE REPORTS

Case of lymphangitis. Abrasion of back of hand two days previously. Rapidly spreading cellulitis of dorsum of hand with several red streaks up arm and lymphadenitis of axilla. There was severe pain in the whole affected area. A. & G. dressing from tips of fingers up to and including the axilla. Splinted, rest in bed, hand elevated on pillow, fluids ad lib. and saline cathartics were additional orders. The dressing was changed daily at the house for two days. In 8 hours the spreading had ceased, the pain practically subsided and the redness and swelling diminishing. In 2 days all the redness and most of the swelling was gone. The man was up and about on the third day, and back to work in 15 days. There was no suppuration or incision.

Case No. 1605, boy, of 14. Infected laceration of thumb; duration 3 days. Infection cleared in 7 days. Discharged with a dry dressing.

Case No. 3470, boy of 12. Infected amputation stump of finger; duration 7 days. Infection cleared in 7 days. Healing sluggish, with necrosis of the edges of the flaps. The wound did not heal completely for five weeks.

Case No. 10214, man. Carbuncle of the neck excised in hospital 6 days previously. Beside the routine treatment it was necessary to control the granulations with silver nitrate crystals. Fourth day, note "Clean wound"; 13th day, dry dressing, wound healing nicely— infection cleared. Discharged healed on the 21st day. (Excision of carbuncles is quite unnecessary with A. & G. treatment). See Case No. 136.

Case No. 136, man. Recurrent abscesses about face and neck. Present condition, carbuncle of neck. Healed in two weeks without incision or excision.

Case No. 11419, man. A boil on the dorsum of the wrist; duration, 2 days. On the third day of treatment the centre slough came away. Fifth day, discharged, with a shallow, clean, healing area; dry dressing.

Case No. 12780, woman. Infected discharging sinus following operation, "Drainage of cyst of the liver"; duration two months. A. & G. instilled into the sinus b.i.d. The discharge practically ceased in four days; the sinus healed in 18 days.

Case No. 13536, a boy of 12. Discharging abdominal sinus. Drainage of an acute appendicitis with general peritonitis. "A very sick boy". Two months later, incision and drainage of a large intraperitoneal abscess in the left lower quadrant; 5 weeks later discharged from hospital. Right incision healed. Considerable thick green pus discharging from left incision, with a large irregular indurated mass subjacent. The boy was seen in out-patient department 3 days later. A. & G. instilled into sinus q.i.d. Five days later discharge no longer green and much less in quantity. Mass, smaller and more rounded. Ninth day, very little discharge; sinus too small to inject for past two days; dry dressing. Sixteenth day, healed, but still a small firm mass below incision. This was not tender. This child was seen six months later. There had been no return of trouble; the wounds were well healed; 24 pounds gain in weight.

Case No. 13435, a boy of 6. Noma of right side of face following typhoid fever complicated by streptococcic bacteriemia. Sloughing of the eye, lower lid, upper part of cheek and osteomyelitis of malar bone. A sequestrum was removed, and he had various treatments during 5 months. When first seen in the out-patient department this note was made. "Purulent discharge in quantity from a sinus passing through the region of the lower lid and into the antrum. A good deal of ex-

cessive granulations. Smear shows many types of infection". A. & G. dressing externally for a week. Discharge lessened and granulations contracted. A. & G. injected into sinus with an eye dropper, t.i.d., and dry dressings applied externally. Alcohol, dram one in glycerine one ounce was used in this case. The progress was more rapid, and at the end of the 7th week wound quite clean. When seen 4 months later there was a small sinus with slight mucous discharge.

Case No. 12861, man. Infected hiatus, $2\frac{1}{2} \times 2$ inches, following excision of a coccygeal (pilonidal) cyst; duration 7 weeks. Little previous progress with various applications. In 3 days wound clean. Healed in 4 weeks. (Many of these cysts and similar defects can be cleared up by sclerosing injections rather than by operation).

Case No. 6303. A girl of 10. Submaxillary sinus following incision and drainage of a purulent adenitis. Duration six weeks. A. & G. applied externally. It was necessary to control the granulations with silver nitrate crystals. Healed in 30 days. (This patient would have done better with instillation of A. & G. into the sinus.)

Case No. 12990, man. Cellulitis of the forefinger; duration three days. The inflammation subsided in six days without pus formation.

Case No. 13364, man. Infected traumatic bursitis of elbow; duration one week. Lymphadenitis extending into the axillary glands. On the third day of the treatment lymphadenitis cleared up; infection localized. Tenth day; dry dressing; infection cleared without pus formation.

Case No. 13564, man. Cellulitis of axilla with abscess formation. Two discharging sinuses and considerable induration eighteen days after incision in hospital. Completely healed in two weeks after reporting to out-patient department.

Case of anal fistula. Man, aged 46. Duration 9 months. The fistula occurred while he was confined in a cast for fracture of the hip. The cast had been opened on the surface three times for abscess formation. The external opening of the fistula was 1 inch to the right and a little anterior to the anus. The internal opening was just above the pectinate line to the right. There was considerable purulent discharge, redness, and induration at the external opening. The sinus was injected 8 times in six days, the faces kept soft with "mucilose". There were no discharge, redness or induration at the end of these treatments. The sinus has healed and remained so for two months. The butt of an ordinary hypodermic needle, after the needle had been broken off, was used on a 2 c.c. syringe for these injections. The syringe was filled twice on each occasion, and the fluid penetrated in the anal canal at the first 5 treatments.

Several cases of impetigo cleared up in from one to two weeks.

A large number of similar cases could be added to this list, but these are sufficient to prove the value of the method.

This mixture causes no irritation of the tissues and can be used in children as freely as adults. This method may be beneficially augmented by dry heat in suitable circumstances. Aseptic precautions must be taken, as far as possible in all dressings. No watery solutions are to be used. The dressings will not adhere to the wounds.

McKim² mentions the use of the dehydrating

effect of glycerine in the treatment of lymphangitis, but only in an incidental manner. In a recent personal communication he says "I may say that I have been using glycerine dressings to a much greater extent than formerly. Sheinkin³ suggests the alternate application of dressings soaked in hot hypertonic saline solution with ones saturated with glycerine "for its antiseptic and hygroscopic properties" to bring forth the pus and sloughs. Kyle,⁴ for twenty years has been using about 25 per cent glycerine in his wet dressings, thus avoiding the bleaching and maceration of the skin. Lichtenstein⁵ comments favourably on the value of glycerine C.P. in suppurative wounds. Glycerine has long been used in combination with other antiseptics in the treatment of otitis media, also for vaginal tampons, etc.

SUMMARY

1. Glycerine combined with alcohol is suggested for the treatment of pyogenic infections generally.
2. It is recommended as being effective, safe, simple, fool-proof and as useful in office practice as in the most up-to-the-minute hospital.
3. The results obtained are illustrated by a series of examples taken from the out-patient department of the Ottawa Civic Hospital.
4. Dehydration of infected tissue is stressed.

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THE TREATMENT OF EMPYEMA THORACIS

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THAT a very active interest is being manifested in the treatment of empyema is evident from the large number of articles upon this subject which have recently appeared in the literature. A study of these reveals the fact that many divergent opinions are expressed and numerous and varied methods of treatment advocated. It is also apparent that undue attention has been paid to details of technique and fads of treatment and too little consideration given to the fundamental principles involved. This is stressed by Graham,¹ Carlson,² Heuer,³ and other recent writers whose statistical studies have done much to change the perspective and transform the attitude of the profession towards this important subject. I shall call attention to certain basic facts which become evident as the result of a physiological, clinical, pathological and statistical study of this problem.

A physiological fact of great importance was first emphasized by Graham and Bell⁴ in 1918, when they showed that if an open pneumothorax is made on one side of the chest, in the absence of adhesions of the lung or fixation of the mediastinum, not only is there a collapse of the lung on that side but there is also compression of the opposite lung due to mediastinal

displacement. If the vital capacity of the patient is lowered by severe toxæmia or pneumonia, this is apt to result fatally. Ewerts Graham (Lewis' Surgery Vol. 14, Chap. 9, page 22) states that when this principle was recognized and the practice adopted of avoiding open pneumothorax during the stage of acute pneumonia in these empyema cases, the mortality dropped from 40 per cent to less than 5 per cent in certain United States army camp hospitals.

There are also certain important facts which have been established by clinical observation. (1) Empyema is not a primary disease but a complication of a pre-existing pneumonia or general infection. (2) Empyema runs a more severe course at the two extremes of life—in the very young and in the aged. (3) There are two clinical types.

Since the influenza epidemics it has been clearly shown that there are two distinctly different clinical types of the disease, the influenzal type and that following lobar pneumonia, which show characteristic clinical and pathological variations. In the influenzal case the empyema is syn-pneumonic and develops while the pneumonia is still active. In those cases associated with lobar pneumonia the empyema is meta-pneumonic, developing after

the pneumonic process has subsided. Another striking clinical difference is the frequency and severity of the complications associated with the former group as compared with the latter.

The pathological differences between these two types are also definite and have an important bearing on treatment. The organism in the influenzal group is usually a streptococcus, while in the lobar group it is a pneumococcus. The pus in the former is thin and watery; in the latter it is thick, creamy, and contains masses of fibrin. Adhesions are scant, weak, and late in forming in the first group, while in the second they occur early and are abundant and dense.

From these facts it is obvious that a different therapeutic approach is necessary in these two types of cases. In the syn-pneumonic case (influenzal), owing to the persistence of the pneumonia and the fact that the patient is acutely ill, possibly suffering from some other serious complication, the minimum operative procedure is indicated, namely aspiration. Further, open drainage is dangerous during the early stage owing to the late occurrence of fixation of the lung. In the pneumococcal group, on the other hand, owing to the early development of adhesions, open drainage is safe almost as soon as pus is present. Moreover as the pus is thick and contains masses of fibrin, it is the preferable method of treatment.

A statistical study of the mortality in several large series of cases of empyema^{1,2,3} has disclosed some rather interesting facts which may be summarized as follows. (1) The mortality varies widely in different years, in different epidemics, and even at different seasons of the year. (2) The mortality varies directly with that of the prevailing pneumonia epidemic. (3) This variation occurs independently of methods of treatment. (4) The mortality varies with the causative organism, being higher in the streptococcal cases than in the pneumococcal, and highest when the *S. haemolyticus* is present. (5) The mortality varies with age, being highest in infancy and old age.

We have been able to corroborate these facts in a review of our cases at the Hamilton General Hospital during the past nine years, as the following tables will show.*

TABLE I
EMPYEMA CASES, HAMILTON GENERAL HOSPITAL,
1926-1934
CASES AND DEATHS ACCORDING TO AGE

Age	Cases	Deaths	Percentage
Under 3 years	31	7	22.0
Under 10 years	72	9	12.3
Including above			
10 to 20 years	19	1	5.3
20 to 30 years	18	2	11.1
30 to 40 years	33	3	9.0
40 to 50 years	18	4	22.0
50 to 60 years	18	3	37.0
60 to 70 years	3	2	66.0
TOTAL	171	24	14.0

TABLE II
VARIATION IN MORTALITY IN DIFFERENT YEARS

	Cases	Deaths	Percentage
Oct., 1926, to Sept., 1927 ...	24	4	17.0
Oct., 1927, to Sept., 1928 ...	17	6	35.0
Oct., 1928, to Sept., 1929 ...	14	0	0.0
Oct., 1929, to Sept., 1930 ...	20	4	20.0
Oct., 1930, to Sept., 1931 ...	14	0	0.0
Oct., 1931, to Sept., 1932 ...	25	6	24.0
Oct., 1932, to Sept., 1933 ...	24	3	8.3
Oct., 1933, to Sept., 1934 ...	33	2	6.0
TOTAL	171	24	14.0

TABLE III
REVIEW OF 79 CASES OF ACUTE EMPYEMA
MORTALITY ACCORDING TO ORGANISMS

Organisms	Number of cases	Mortality	percentage
<i>Pneumococcus</i>	32	3	9.4
<i>Pneumococcus</i> and <i>S. haemolyticus</i>	11	0	0.0
<i>Pneumococcus</i> and <i>Staph. aureus</i>	2	0	0.0
<i>Pneumococcus</i> predominates in	45	3	6.6
<i>S. haemolyticus</i>	11	2	18.0
<i>Staph. aureus</i>	3	0	0.0
<i>Staph. aureus</i> and <i>S. haemolyticus</i>	4	0	0.0
No growth	2	0	0.0
No record	14	4	

These facts emphasize the importance of active treatment of the primary infection and of efficient general supportive treatment of the patient, as well as the relative unimportance of fads of technique, so far as the mortality is concerned.

We must now consider what are the objectives to be attained in the treatment of empyema, and in the light of the facts just presented define the best method of attaining these objectives. The objectives may be stated as follows: primary. (1) to save life, (2) to prevent chronicity; secondary, (1) to shorten convalescence, (2) to prevent deformity; and (3) to restore function.

* I wish to thank Dr. R. E. Nicholson and the Record Department of the Hamilton General Hospital for their cooperation in obtaining these statistics.

Before formulating rules regarding the saving of life it will be profitable to consider the causes of death. The following information is compiled from several recent articles and from our own records. I have classified these into three groups as follows.

TABLE IV
CAUSES OF DEATH IN EMPYEMA

- | |
|--|
| 1. The severity of the primary infection: (a) septicæmia and pyæmia; (b) pneumonia, abscess of the lung, gangrene of the lung. |
| 2. Serious complications, <i>e.g.</i> , meningitis, pericarditis, etc. |
| 3. Those dependent upon the operation: (a) shock; (b) open drainage in the formative stage; (c) infections of the chest wall. |

It would appear that the control of the causes in the first two groups depends almost entirely upon the active treatment of the infection and the general treatment of the patient.

The cause of death in the third group can be largely controlled by carefully adapting the operative procedure to the tolerance of the patient, taking into consideration the age, the activity and the severity of the general infection and the complications present. Secondly, the type of operation must be selected according to the stage of the disease, open operation being avoided in the formative stage.

As regards chronicity, in order to deal intelligently with its prevention we must be familiar with the causes which give rise to it. These may be summarized as follows: (1) failure of the cavity to become obliterated; (2) persistence of infection.

These unfortunate results are due largely to causes which can be conveniently divided into three groups, as follows: (1) undue delay in treatment, causing (a) an unduly large cavity, (b) dense adhesions, (c) fibrosis of the lung from prolonged compression; (2) inadequate drainage; (3) miscellaneous, as bronchial fistula, foreign body, necrosis of the ribs, etc.

It is apparent that most of these conditions are preventable and the responsibility for their occurrence, with the exception perhaps of bronchial fistula, rests rather heavily upon the shoulders of the medical attendant.

The essentials as regards the prevention of chronicity may be stated briefly as follows: (1) early evacuation of the cavity, (2) measures to promote re-expansion of the lung, (3) adequate drainage.

We may now briefly review the various methods of treatment which have been advocated.

These are: (1) Simple repeated aspiration. (2) Aspiration with, (a) antiseptic irrigations, *e.g.*, bile salts, (b) air replacement. (3) Closed drainage; (a) with Carrell-Dakin irrigation. (b) with pneumothorax of opposite side. (c) with suction or negative pressure. (4) Open drainage: (a) intercostal incision, (b) rib resection, (c) wide thoracotomy with packing. (d) flap method.

Aspiration alone may cure a certain number of cases. McEnery and Brenneman⁵ report a series of 94 cases with 70 per cent of cures by aspiration alone, and a mortality of 12.8 per cent. They state however that they are now employing open drainage more frequently.

Aspiration with air replacement has as its rationale the early evacuation of the effusion and the prevention of the too rapid expansion of the lung during the acute pneumonic stage. As the air is gradually absorbed it encourages a gradual re-expansion of the lung. Using a 30 c.c. syringe, as a syringe of pus is aspirated it is immediately replaced by air and this procedure is repeated until no pus returns. This is carried out again in four or seven days (Bloch and Parrish⁶). Danna⁷ reports a series of 35 cases with no deaths, but states that 5 required subsequent open drainage.

Aspiration with the injection of bile salts (Sod. desoxycholate) has been advocated in pneumococcal cases, and Sworn and Cooper⁸ report 3 cases treated and cured by this method. The technique consists in aspirating and demonstrating pneumococci, and then aspirating as much pus as possible, followed by the injection of 5 to 20 c.c. of 5 per cent Sod. desoxycholate solution. This is repeated daily or every second day. A progressive diminution of pneumococci in the exudate is noted.

Recently artificial pneumothorax on the opposite side has been advocated, after establishing closed drainage.⁹ The idea is to promote expansion of the compressed lung by throwing more work upon it. This may have value in the post-operative treatment of empyema in the hastening of the re-expansion of the lung.

As regards wide thoracotomy with packing, advocated by Connors,¹⁰ while this method seems unnecessarily radical for most cases it is

definitely indicated in the interlobar type of empyema, which for purposes of treatment resembles a lung abscess. Here, if the visceral and parietal pleural surfaces are not adherent, a two-stage operation must be carried out. In the flap method, described by Nicholl¹¹ in which a valve arrangement is constructed by means of a skin-flap, it is claimed that free exit of pus is permitted and entrance of air on inspiration prevented.

While many ingenious and complicated methods of treatment are described, space does not permit their detailed description. Only a few simple procedures are necessary in actual practice, but these must be applied in accordance with the principles we have just enunciated. The old dictum *Ubi pua ibi evacua* must be qualified in the case of empyema. While too early open drainage may be disastrous undue delay is also undesirable. Those late neglected cases of *empyema necessitatis* where the pus points beneath the skin should never be seen with modern methods of diagnosis. We will briefly outline those therapeutic procedures which we believe are of importance and point out the indications for their use.

The importance of early and active treatment of the general infection is of paramount importance. Anti-streptococcic or scarlet fever serum in the influenzal cases, and pneumococcic serum, according to type, in the lobar cases, should be used. Blood transfusion, especially in children, is a valuable procedure. In fact every child with empyema should be grouped and a donor procured. Frequent small transfusions are of great value. Transfusion with immune serum, where the donor is previously inoculated with a vaccine prepared from the patient's pus, is lauded by Fraser¹² and others. Of equal importance is the maintenance of the general resistance by adequate fluid and caloric intake. Many of these patients, especially children, take very little in the way of nourishment, and fluids and intravenous glucose and saline should be used more frequently. If we treated these patients half as intensively as we do our pre-operative prostatic cases or our post-operative peritonitis cases, I am certain our results would be better. As soon as the vital importance of combating the primary infection is driven home, together with the point of view that the empyema is only a complica-

tion and not the primary disease, our results will improve.

As regards local measures, aspiration should always be the first employed. As a diagnostic procedure it is essential in demonstrating the presence of pus, its character, the organisms present in smear and culture, and the pressure registered by the exudate.

Therapeutically, aspiration is invaluable for relieving respiratory embarrassment and also for ridding the patient of some of his load of toxæmia. It should be repeated as often as indicated, to tide the patient over the critical stage of his illness, while the pneumonia is still active and until fixation of the lung and mediastinum have occurred. It is also helpful in preventing the development of an unduly large cavity which would be difficult to obliterate, and in avoiding such prolonged compression of the lung as might lead to fibrosis and dense adhesions with the prevention of re-expansion. While aspiration is used with these objects in mind, it must be admitted, as previously mentioned, that it will cure a small percentage of cases. When the pus is diminishing and becoming thinner and the temperature is falling it may be persisted with, in the hope of obtaining a cure.

Certain precautions must be observed in the use of aspiration. The too rapid and too complete removal of the exudate should be avoided, especially during the early stages and in syn-pneumonic cases. We must remember that the exudate exercises a beneficent influence in providing rest for the inflamed lung. It is conceivable that the use of air replacement with aspiration as recommended by Danna⁷ will prove of value in preventing too rapid expansion of the acutely inflamed lung and at the same time permit of the complete removal of the exudate.

Accidents have been reported following simple thoracentesis, and these have been attributed to pleural shock. It is much more probable that they are due to air embolism.¹³ While a considerable quantity of air may enter the systemic veins without a fatal result, a comparatively small amount entering the pulmonary veins will cause convulsions and even death.

Undoubtedly, most cases of empyema eventually require operation, but we cannot emphasize too forcibly that operation is never an emer-

gency procedure, as these cases can always be relieved temporarily by aspiration. Open operation should not be carried out until the pneumonia has subsided and the lung become fixed by adhesions. In other words, operation should be deferred until we are dealing with a closed cavity, of which the most certain evidence is the fact that the pus registers a positive pressure during aspiration. Complicated types of apparatus and ingenious methods of operation, although continually devised, are not only unnecessary but futile. The only operative measures which need be considered are those mentioned below which have stood the test of time, and the results of which so far have not been surpassed by the most bizarre mechanical devices or dexterous operative manipulations. Closed drainage by means of trocar, cannula and catheter is a simple procedure which can be done painlessly under a local anæsthetic, in the patient's bed and in his own home if nursing care is available. It is indicated in patients who are very ill, possibly with a septicæmia or some serious complication. It is preferable in the very young and in the aged. It is also safer when there is any uncertainty as to the presence of fixation of the lung. When employed, it must be given careful supervision. It must be used in conjunction with Carrell-Dakin irrigations (one-third to one-half strength), which not only keep the tube patent but liquefy the masses of fibrin in the exudate and help to dissolve adhesions and fibrinous exudate on the pleura. This is contraindicated if the patient coughs or tastes the solution after injection, as this indicates the presence of a bronchial fistula. It is well to use saline for the first injection and if no evidences of fistula exist then carry on with the Carrell-Dakin solution. Drainage should be continuous, and the tube clamped only for fifteen or twenty minutes after the four-hourly instillation of the Dakin solution. By noting the quantity of solution which the cavity will contain as the solution enters by gravity its progressive diminution in size can be followed. Tidal irrigation is a modification of this method but does not possess any advantages over the above method.

Open drainage has very definite indications and contra-indications in the treatment of empyema. It is unsafe before fixation of the

lung and mediastinum have occurred, and in patients who are very ill, especially children, is not advisable. If the patient is tided over this stage by aspiration then open drainage possesses certain advantages. It requires very little supervision, and one is certain of an adequate exit for the pus. It is the method of choice in pneumococic cases where the pus is thick, and after fixation has occurred, with a patient in reasonably good condition. It is also indicated where closed drainage is not successful and fails to bring down the temperature and produce satisfactory clearing-up of the infection.

Certain details of technique are worth noting. In the first place never resect a rib until you have first located and obtained pus by aspiration on the operating table just prior to your operation. Sometimes the pus is present in pockets and must be accurately localized before the drainage opening is made.

The site of the opening is of great importance. It should be in the 8th interspace in the posterior axillary line, or just behind this. The angle of the scapula, when the arm is by the side, overlies the 7th space, and if the opening is made higher the scapula and its muscles interfere with drainage. On the other hand, if the opening is made lower, with the ascent of the diaphragm and the obliteration of the costophrenic angle, which always occurs, the opening will be obstructed.

The tube should be marked in inches so that the exact distance of insertion can be easily determined, as the opening may be above the puddle of pus. This applies particularly to cases where closed drainage is being used. I am also in the habit of making an additional lateral opening in the tube near its inner end.

Both trocar and catheter drainage and rib resection can and usually should be done under a local anæsthetic.

CONCLUSION AND SUMMARY

1. The mortality in empyema depends largely on the virulence of the primary infection, the organism concerned, and the complications present.

2. Apart from the danger of open thoracotomy in the formative stage and of exceeding the patient's tolerance for surgical interference, mortality is influenced very little by methods of treatment.

3. Chronicity is more directly dependent upon the time and type of the therapeutic procedures employed.

4. While some of the complicated methods of treatment may have a limited application in the treatment of empyema, if the fundamental principles involved are observed variations in methods have little effect upon mortality.

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AUTOGENOUS SERUM TREATMENT OF NARCOTIC ADDICTION

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A NEW treatment for narcotic addiction has been gaining increasing popularity throughout the Orient during the past few years. On the basis of a number of cases successfully treated in the Canadian Mission Hospital, Lungchingsun, I thought that it might be of value to bring the method to the attention of physicians in Canada.

The treatment was originated in Java by Dr. Modinos, and consists of the subcutaneous injection of autogenous serum taken from a blister raised with the aid of a cantharides plaster. It is based on the theory that there is an antidotal toxic substance in the serum of addicts. It has a remarkable effect in reducing the withdrawal symptoms and the craving for the drug in those addicted to opium, morphine and heroin. I do not know if it has been tried in cases of addiction to cocaine or other drugs. The method was brought to our attention by an article by Dr. Lee S. Huizenga.¹

Before beginning the use of autogenous serum we had a considerable experience over a number of years in treating cases of opium and morphine addiction by gradual withdrawal. It was our custom to give decreasing doses of tincture of opium in combination with tincture of belladonna and tincture of nux vomica. As we have

no facilities for the strict control of patients the withdrawal had to be gradual and based on the cooperation of the patient. Most were treated in the open ward. We have continued this method, but by using the injections in addition have been able to reduce both the time required and the discomfort suffered by the patients.

METHOD

On admission the patient is given a physical examination, and is told that he will have some discomfort, but is promised that it will not be more than he can stand. His cooperation is solicited; in fact, he is told that the cure depends entirely on him. An estimate is then made of the amount of narcotic which he has been taking, and he is given enough tincture of opium by mouth on the first day to nearly equal his customary dose. This varies from 3 c.c. to 25 in twenty-four hours, usually divided into four equal doses.

A plaster is then prepared by taking a four-inch square of adhesive plaster, to the centre of which is applied enough Emplastrum Cantharidini B.P. to make a circle one and a half inches in diameter and about one-sixteenth of an inch thick. The skin of the upper abdomen is cleansed with alcohol and the plaster applied.

The patient is warned to avoid breaking it, and it is left in place from eighteen to twenty-four hours. It causes some pain, but very few of the patients have complained very much about the discomfort. If complaints are made the plaster may be removed after about six hours and the site fomented to raise a blister. This is, of course, much more troublesome and there is a danger of bursting the blister, but it may be necessary in sensitive patients.

When sufficient fluid has collected in the blister or, in any case, at the conclusion of twenty-four hours, the blister fluid is taken up in a syringe and injected subcutaneously. The fluid may be collected in several different ways. The blister may be broken and the fluid collected in a sterile dish, or the edge of the plaster may be raised and the needle passed into the blister from the side. The simplest method, however, and the one which involves least danger of losing any fluid, is to plunge the needle straight through the centre of the plaster, which is first painted with an antiseptic. In using this last method it is wise to change the needle before making the injection, to reduce the danger of introducing the irritant cantharidin beneath the skin. The injection of the blister fluid would appear to involve some risk of infection, but we have not met with any infections in our cases.

The amount of fluid obtained from a blister varies greatly. Some skins are much more sensitive than others, and, depending on the result of the first blister, it may be necessary to increase or decrease the size of subsequent plasters. We have injected as much as 10 c.c. of blister fluid, but a dose as large as this sometimes causes some reaction and discomfort. Probably the optimum injection is about five or six c.c., though even as little as 1 c.c. has an appreciable effect.

The blister site heals in a few days without trouble. We have found a 5 per cent solution of tannic acid effective as a dressing. It is better, if possible, to leave the loose skin in place after removing the plaster. Another blister is applied the day after the injection, and further ones every second or third day as required. We have not found it necessary to give more than four injections of blister fluid to any one patient. In the meantime tincture of opium is continued in rapidly decreasing doses, combined with tincture of belladonna and tincture of nux vomica. Phenobarbital or nembutal are given to assist in

obtaining sleep. The bowels are kept open with compound cathartic pills, three or four of which are needed in a dose at the outset of treatment.

SUMMARY OF CASE REPORTS

We have records of 17 patients who were given this treatment during 1935. Two of them discontinued treatment, both within the first two days before there had been a chance for the injected serum to assist in giving relief. As noted above, all the patients were treated on an entirely voluntary basis. The remainder all reached the stage where they had been quite comfortable without their drug for a period of several days before discharge from hospital. Because local conditions make follow-up work very difficult we are unable to report on the after-histories of the patients.

Of the 15 patients who completed treatment 7 were Koreans and 8 were Manchurians (Chinese); there were 8 males and 7 females. One had smoked opium for twenty years; 5 were taking opium by the mouth; 5 were using morphine and 2 heroin subcutaneously; 1 was taking six intravenous injections of morphine and 1 four intravenous injections of heroin daily. With the uncertainty of weights and measures obtaining here it was very difficult to estimate the exact amounts of the drugs which the various patients were using. Some were light cases but some were decidedly heavy addicts. The duration of the habit varied from two months to twenty years with an average duration of 3.7 years.

One patient received four plasters and injections; 8 received three injections; 5 received two injections; and 1 patient had only one injection. The average number of days before the opium was entirely discontinued was 7. We found ourselves tending to cut down the opium very much more rapidly in our later cases than we had done in the earlier ones. One severe case was given two injections of morphine early in the treatment. All the rest received only tincture of opium by mouth. After discontinuance of the opium sedatives were given for several nights, a tonic given, and an attempt made to treat any underlying conditions. In only one case did we have any trouble with diarrhoea setting in after withdrawal.

THE EFFECTS OF THE INJECTIONS

In every case the injections were followed in a few hours by a lessening of discomfort and a decrease in the craving for the drug. Some of our patients refused opium after their second injection. Reports from China^{2, 3} claim that the treatment gives rise in some cases to a definite aversion to the smoking of opium and to a distaste to the drug by mouth. We have not definitely confirmed this. It does not have any such positive effect in the case of drugs taken by injection. The patient can be cured and definitely relieved of his craving, but if he starts injections again he will relapse.

It has been suggested by Mumford⁴ that auto-hæmotherapy is also an effective means of treatment. We have not yet had any experience with it.

SUMMARY

An account is given of experiences in treating fifteen cases of narcotic addiction by the

Modinos method of injecting autogenous serum obtained from blisters. It allows of much more rapid and less painful withdrawal, and has a definite effect in relieving the craving for the drug.

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AN ELEMENTARY CONCEPTION OF THE NEUROSES

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THERE is, perhaps, no topic of greater importance in the whole wide realm of psychiatry than that of the neuroses. It should be clearly realized however that neuroses exist not only in hospital wards and out-patient clinics; in world affairs and even in the non-professional side of social life the transcendent importance of faulty mental attitudes is borne in upon us.

When one realizes that 50 per cent of hospital beds are occupied by patients suffering from mental disorders, that varying estimates of Out-patient Departments (admittedly inaccurate) give the percentage of neuroses as from 40 to 60; that in 1932 Canada cared for 35,279 mental patients at a cost of over \$11,000,000; when one realizes that there is no index of the amount of human misery and inefficiency arising from purely psychogenic sources, the urgency of the problem seems beyond cavil. To emphasize the importance of such a topic is merely to labour the obvious, and might seem to suggest an apologetic attitude for one's choice of subject, which is not intended.

No term is more frequently used in everyday medical talk than "neurosis", and no term has wider and vaguer connotation. As a very convenient repository for many of our diagnostic difficulties and, alas, many of our therapeutic failures, it has, perhaps, a certain dubious value; as a fascinating, if very troublesome, problem it presents an urgent challenge which cannot be refused.

Annandale's dictionary defines "neurosis" as "a disease which has or is said to have its seat in the nervous system". Such a definition can hardly be said to be illuminating, yet much of our medical and psychiatric teaching is of little greater value. Around no other topic is the

literature more voluminous, the controversies more acrid, the thinking more vague, and the multitudinous claims so ill supported. Much of this sorry state of affairs is attributable to the numerous widely varying modes of attack on this baffling problem. Each group, anatomical, physiological or biochemical; behaviourist, integrative or psycho-analytic; is represented, far too often, by fanatics crying their own wares in the market place and endeavouring to discredit all rival vendors. Indeed, as someone has well said, the psychopathology of psychopathologists would of itself form an interesting topic.

Roughly speaking, there are two main schools of thought—on the one hand, what may be called the neuro-physical group stressing the somatic aspects; on the other, the psychological emphasizing the dynamic mental factors. There is no time to debate the relative merits of the two schools, nor indeed is it necessary to do so. It is obvious that there is no fundamentally exclusive solution in favour of the one or the other. Each is a laudable attempt to gain sorely needed knowledge, and to set one against the other, as if mutually antagonistic, is a totally unjustifiable though regrettably common procedure—a carry-over, it would seem, from the mediæval body-mind controversy. It is high time that the concept of organismal unity were given more than lip service.

Graham Howe has an apt analogy in his recent monograph which is worth quoting. "Let us", he says, "imagine we are working a magic lantern, which projects on the screen a blurred, confused, quite unintelligible picture. Parts are clear, but seem to have no connection, and the whole picture seems to be produced by several overlapping slides. Perhaps some helpful individual comes to our assistance and selecting one slide, holds it up saying, 'There, see how

* Read before the Psychiatric Section of the Montreal Medico-Chirurgical Society, on October 22, 1935.

clear it all is — a straightforward Inferiority Complex', and so perhaps it is. But far more often, another picks up another slide and says, 'No, an Oedipus situation and those things are phallic symbols'; and then another and another selects other slides and makes each his separate claim — 'Recapitulation mechanism' — 'Thinking extravert' — 'Hyperthyroid with an over-active autonomic system' — 'Toxic; look at his teeth and tonsils'. So the babel and confusion increase to Alice in Wonderland proportions, for each sees only his own slide, whereas in truth each is but a component in the original confused picture, the picture of a man's life." Little wonder, the perplexity engendered by a problem of such dimensions. For purposes of brevity the remainder of this paper will be confined mainly to the psychological aspects of the neuroses.

In any discussion, it is wise to define terms, and no term is more sorely in need of definition than "neurosis". What is a neurosis? Stripped of all the redundant verbiage with which we endeavour to cloak our ignorance, what do we mean by neurotic behaviour? Easy is it to pose such a question but not so simple to frame an answer, for it raises the whole tremendous issue of mental health and all its concomitant problems. It is the writer's feeling that in the present state of our knowledge we can go no further than to say that any behaviour that interferes with the attainment of a reasonable degree of personal happiness and social efficiency may justifiably be classed as neurotic. Beyond this bald statement are a myriad provocative suggestions, but certainty, even security, are far to seek. The will o'the wisp of nebulous theory has lured too many into the marshes of confusion already.

Granting such an admittedly vague and unsatisfactory tenet, why do individuals adopt this type of reaction to the difficulties of life? Admittedly, neurotic pain is as real as the pain of organic disease, and yet all of us believe that the cause of that pain resides in the mind, the psyche, of the patient. What is the explanation? Is the pain imaginary or due to conscious stimulation? Few, if any, can derive any satisfaction from such a view, so empty and meaningless is it.

If then imagination and conscious feigning merely beg the question, can any more satisfying view be put forward? Only one has received almost unanimous support, namely, that

in some way these symptoms are of advantage to the patient — through them some goal, otherwise unattainable is reached. In other words *neurotic symptoms are purposeful*. It is probably true that certain mental symptoms such as the depressions of chronic infection, the toxic and exhaustive states, the febrile deliria are resultants of some antecedent cause and subserve no end in themselves. Louis Minski's recent study on brain tumours shows clearly how the mental picture is merely an exaggeration of the pre-existing personality type, and certainly suggests that strictly organic factors may be utilized to further the ends of that individual. Each psychogenic symptom should be considered from both resultant and purposive aspects.

It should be noted that certain organic symptoms can also be regarded from this aspect. The tremor of paralysis agitans, the ataxia of cerebellar tumour, are obvious sequelæ of recognized demonstrable pathological changes and subserve no end in themselves. Vomiting, however, though it may be the direct result of a high intracranial pressure, is often an attempt to rid the organism of some noxa which threatens its well-being. The redness, the heat, pain, swelling and loss of function in an inflammatory process is certainly the resultant of some infection, but is it not also a purposive attempt on the part of the organism to defend itself against that infection? In both organic and psychogenic fields it should be noted that—

1. The symptom, albeit purposeful, is utterly beyond the field of conscious control. No man by taking thought, can add one cubit to his stature, nor can he call forth his leucocytes by any conscious effort of will.

2. The process, whether psychogenic or organic, is not self-limited, but will, if untreated, continue to the detriment if not the destruction of the organism.

This distinction between resultant and purposeful symptoms, or, perhaps, more correctly, between the resultant and purposeful aspects of certain symptoms is not unimportant. Not only does such a view tend to clarify thinking, to some extent at least, but it also suggests that therapy may be applied from two angles, on the one hand attempting to find and deal with the causal factors, on the other, aiding the patient to recognize and deal with his difficulties in some more mature and satisfactory fashion. Freud's classification of the neuroses into the

true neuroses (anxiety neurosis, neurasthenia) and the psychoneuroses (hysteria, etc.) may perhaps be considered as following the same plan. The true neuroses are not considered as amenable to analysis but as disorders of the psychosexual life only to be treated by an adjustment of that aspect, and therefore could be regarded as resultant, while the psychoneuroses are subjected to analysis in an endeavour to uncover for the patient those instinctive urges which have been expressed in his symptoms. These symptoms then are purposive, albeit unconscious, attempts to gratify these basic urges. Whether one is entirely prepared to accept the Freudian classification is a topic not germane to the present discussion.

Now, if certain neurotic symptoms are purposeful, that is, designed to attain some unrecognized but greatly desired goal, what can these ends be?—ends so desirable, goals so alluring that even illness, crippling, torturing, disabling illness, is preferable to their renunciation. To attempt to define the manifold desires of mankind is to lay oneself open to the most stringent and well deserved criticism. Still, if it is expedient at times that one man should die for the people, one may dare, perhaps, to immolate oneself on the altar of sacrifice and offer a tentative formulation which may serve to focus discussion. Following Graham Howe's classification, there are three primary urges, which must be satisfied if a mature healthy adaptation to life is to be attained. These are:—

1. Love.—This is most interestingly defined as the need for priority; a distinctly unusual view and one most provocative of consideration. The mother whose headaches keep her children dancing attendance on her; the jealousy of the lover; both these may be thought of, in part at least, as expressing the need to come first in someone's life.

2. Protection.—The need for security. This needs no further expansion. The obvious efforts of children, whether their actual age be three or thirty-three, to attain safety and certainty, both in the family situation and outside it, furnish examples well known to all of us.

3. Power.—The need for control. The all-too-frequent attitude of teachers, parents and all those set in authority over us render comment superfluous. It is not suggested for a moment that any one case can be forced into any one category, but merely that this scheme may serve

as a convenient framework and maintain a little sorely needed order in the tangle of the neuroses.

If these urges or desires do not attain some reasonable modicum of satisfaction then the individual, realizing consciously or unconsciously his lack, *must* adopt some means of compensating for that lack. The whole process is tragically inevitable. Each individual must compensate for the deficit in these three basic needs. The mechanism of that compensation need not necessarily be the painfully unsatisfactory one of the neurosis, but far too often such is the outcome. To quote Howe verbatim, "The illness is a means to an end, and the end is love, protection and power, any or all. It is therefore, not true to say that the patient desires his illness as such. He does not, but desires it as a means to satisfy his needs. He is not conscious of his needs, but love, protection and power are goals which human nature is pre-ordained to seek and find attractive".

It is suggested then that the neurotic be considered as an individual reacting to difficulties in his personal life in a certain definite, comprehensible way. The method selected, albeit unconscious, is one that interferes with the attainment of a reasonable degree of personal happiness and social utility by that individual. Here perhaps lies the real discrepancy between the neurotic and the healthy individual. Each reacts to the difficulties of life in a certain definite individual fashion. The procedures are identical, the results as far apart as the poles. The one meets his difficulties with a certain amount of objectivity, recognizing and accepting his own shortcomings, attaining at least some degree of happiness and content—a useful productive member of society; the other flees from his problems, adopting some transparently immature device to cover his evasion—unhappy, timid, a source of torment to himself and to those about him, a non-productive liability to the social order.

Now, if the two procedures are identical and yet the outcome so divergent, wherein lies the essential difference? Obviously, there are but two factors involved, first, the individual original endowment, personal and ancestral, with which each sets out on his way through life, secondly, the varied experiences encountered. There is no place here for a recapitulation of the hoary heredity versus environment argument. Of the

former we may well say with Kipling, "we are distracted by what we have proved, we are afflicted by what we know". Certainly it is not in our power, as physicians, to influence this tremendously important factor, though the rapidly accumulating work of the geneticists augur better things for the not too distant future. Freud's dictum, that certain individuals would have become sick (*i.e.*, neurotic) in any case, while others would have come through unscathed under more favourable circumstances, still covers the situation quite adequately.

In purely pragmatic terms, then, the only procedure is, seemingly, to concentrate effort upon the alterable environmental factors. Perhaps, a warning note may not be out of place at this juncture. There has been a vast amount of uncritical acceptance of distinctly dubious diets in the psychological field; more, though perhaps not so very much more, than in other aspects of medicine. It is high time that psychological tenets were subjected to the dispassionate scientific appraisal which has ever characterized the progress of true investigation. The whole field of psychopathology is complicated by claims for panaceas resting on foundations unsound to a degree. Generic solutions of extremely intricate problems are offered with a glib facility hardly conducive to critical acceptance. On the other hand, an equally unreasoned purely destructive criticism and resistance has proved equally disturbing. The obvious emotional (unconscious) motivation of these attitudes would form an interesting study of itself, but would be out of place in this paper. Granted the obvious drastic criticisms which can be and are advanced so freely, the equally striking progress in this field can hardly be denied.

If then the attack is to be centred on the environmental factors, to say that much further research and study is required seems merely labouring the obvious. In this connection it must not be forgotten that the internal environment, the physiological functioning of the organism, is at least as important as the external surroundings. The consistent findings of numerous metabolic and endocrine anomalies in the mentally ill, the question of focal infection, and

many other problems cannot be ignored. These, of course, merely serve to drive home the age-old dictum of the unity of the organism. To say that the whole man must be treated is to perpetrate a truism of the worst type, for which apology must be made, though practice hardly follows precept to completeness in this matter. Certainly, the utmost resources of clinical medicine in its broadest aspects are not too great to be mobilized to aid in the attack on a problem of this magnitude.

In this connection two points, relatively minor perhaps but still too frequently neglected, should be touched on. It is far from uncommon to encounter patients whose symptoms are directly related to the unthinking words or even attitude of a physician in a previous examination. True that other symptoms would probably have been adopted in any case, but even so it would seem a point worthy of emphasis. Closely allied is the unconsidered use of clinical procedures. The aura of mystery and terror surrounding the darkened fluoroscopic room or the electrocardiograph is not devoid of effect upon a suggestible patient. It is hardly necessary to say that all essential examinations must be carried out, but often where the clinical picture is obviously that of neurosis these procedures are embarked upon with little if any consideration of their possible effect on the patient. Such an attitude imposes added responsibility on the physician but cannot be ignored much longer. Endeavouring, as we do, to make the patient evaluate his symptoms as the result of faulty mental attitude, the educative value of removing emphasis from the secondary somatic elements may not be entirely worthless.

Time, the writer's ignorance, and an element of consideration for his readers, combine to prevent any discussion of the fascinating topics of symptom-formation and therapy in the neuroses. The writer's endeavour has been to bring forward a few points which may lead to a clearer conception and so to a more adequate attack on the vast problem of neuroses. Should this paper, in some measure, serve to stimulate interest and discussion in this neglected but vitally important subject it will have served its purpose.

THE EFFECT OF REPEATED INJECTIONS OF CHOLINE AND *B. PYOCYANEUS* IN THE DOG

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HALL, Ettinger and Banting¹ have reported severe myocardial and coronary arterial damage in the dog as an effect of repeated and prolonged intravenous administration of acetylcholine. Death from cardiac failure occurred in from 26 to 235 days. In order to determine whether this damage was due to the choline formed by the rapid hydrolysis of its acetyl ester, the experiments were repeated on two dogs to which choline was administered in place of acetylcholine. Even choline would have a very fleeting effect, as Hunt² has shown that it is removed from the blood-stream within a minute after injection.

METHOD

Two male dogs weighing 30 and 32 lbs. were used. Preliminary determinations were made of normal temperature, respiratory rate, heart-rate, blood pressure (Dameshek and Lomann's method) electrocardiograms, red blood-cell count, hemoglobin, blood-culture and body weight. Approximately the choline equivalent of the acetylcholine used in Hall, Ettinger and Banting's experiments, viz., 45 mg. of choline chloride, was dissolved in 500 c.c. of sterile normal saline, and injected from a sterile Mariotte cylinder into a leg-vein at a steady rate which required 90 minutes for the complete injection. This was repeated daily, without anaesthesia. The heart-rate and sounds and respiratory rate were observed during the injection. The rectal temperature was noted each day before injection. The other preliminary observations were repeated weekly.

In the acetylcholine experiments the dog which had the most severe coronary and myocardial damage died within thirty days of the onset of the experiment and

had a terminal blood infection with *B. pyocyaneus*. It was therefore decided to seed the choline solutions with this organism for the early part of these experiments. This was done for four months; thereafter the usual sterile precautions were observed.

RESULTS

The injections were given six days in the week, over periods of 153 days (131 injections) and 231 days (198 injections), during which the dogs were well, had normal appetites, and gained in weight. There was no change in the heart rate during the course of an injection. There were no murmurs nor other clinical evidence of any disturbance or impairment of the cardiovascular system during the course of the experiments. For the first six weeks of the four months during which the solutions were heavily contaminated with *B. pyocyaneus* the bacteria could be recovered from the blood; thereafter the blood was sterile. On the day after the last injection the animals were killed with chloroform. Careful autopsy, including macroscopic sections, failed to show any degenerative changes in the myocardium, coronary arteries of the heart, or in the blood-vessels of any other organ.

CONCLUSION

Daily intravenous injection of 45 mg. of choline chloride solution over periods of 153 and 231 days caused no degenerative changes in the heart of the dog. Heavy infection of the solution with *B. pyocyaneus* for four months of these periods did not affect the heart or its blood-vessels.

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SEASONAL CHANGES IN THE BLOOD.—C. Hampf has investigated in Helsingfors the composition of the blood at different times of the year. In one series of observations 22 healthy adults (11 men and 11 women) were examined systematically monthly for a year. Their ages ranged from 23 to 54. The hemoglobin content of their blood was over 75 per cent (Sahlbi) in the case of the men, and over 70 per cent in the women. The samples were taken in the morning fasting. It was found that during the winter months the number of the erythrocytes was about 100,000 lower than in the summer months in both sexes. The percentage of hemoglobin followed a parallel course, being about 4 per cent lower in the winter than in the summer. There was only a small rise in the winter months in the number of the leucocytes, but there was a significant change in the neutrophile

count, the cells with rod-shaped nuclei rising abruptly in numbers in the spring, and reaching the maximum level in June in both sexes. In women the eosinophiles reached their maximum number in April. In a second series of observations the author has collected the 4,375 complete blood counts undertaken in his hospital in the period 1930-5, devoting special attention to the 558 counts uninfluenced by such factors as might have a specific effect on the composition of the blood. No uniform seasonal change was demonstrable in the number of the erythrocytes, and the percentage of hemoglobin varied proportionally with this number. The author is inclined to believe that, as far as Finland is concerned, the seasons of the year impose no profound changes on the blood count.—*Finska Läkaresällskapet's Handlingar*, February, 1936, p. 141. Abs. in *Brit. M. J.*

THE EFFECT OF REPEATED INJECTIONS OF HISTAMINE IN THE DOG

A. ON THE HEART AND BLOOD-VESSELS

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HALL, Ettinger and Banting¹ (1936) reported that repeated and prolonged daily intravenous administration of acetylcholine in the dog may, in a period of from 26 to 235 days, cause severe myocardial and coronary arterial damage. During the period of injection the drug caused visible profuse vasodilatation, salivation, vomiting, bowel-movement, and a tachycardia which doubled or trebled the normal heart-rate. All the animals developed systolic murmurs a considerable time before their death, which invariably appeared to be due to cardiac failure.

In order to determine whether the degenerative changes in the heart were due to a specific toxic effect of acetylcholine, or were the combined effects of the low blood-pressure and the accelerated heart, the experiments were repeated on three dogs, using histamine in place of acetylcholine. A contributing factor might lie in the prolonged action of the drug on the coronary arteries. Acetylcholine is generally assumed to cause coronary vaso-constriction, but there is equally good evidence (Narayana²) that it may cause dilatation. Histamine is credited with causing coronary arterial constriction in the dog (Anrep,¹ Cruickshank and Subba Rau²), and also dilatation (Rühl,¹² Müller, Salomon and Zuelzer⁸).

SELECTION OF ANIMALS

The continuous intravenous injection of a solution of histamine is not accompanied in all dogs by a continuously accelerated heart. Since it was essential for these experiments that a high heart-rate be maintained throughout the period of injection careful selection of the dogs was necessary. In one animal under urethane, and in six animals without anaesthesia, the continuous intravenous injection of histamine acid phosphate, 1/10,000, at the rate of 2 to 4 c.c. per minute, produced considerable acceleration of the heart lasting for only about 2 minutes, after which the rate was little, if at

all above the normal, even though there was flushing, vomiting and (as seen in two animals, one under urethane and one without anaesthesia) a continuous depression of the blood-pressure of 35 to 50 mm. of mercury. An eighth animal showed profound cardiac acceleration, which seemed to increase as the injection progressed; this animal was selected for the experiment. Two other animals were also used. One of these had had the right vago-sympathetic nerve cut shortly before; he showed a prompt and continuous cardiac response to histamine. The right vagus nerve was then cut in a third dog, one which had previously been refractory. This animal now showed continuous cardiac acceleration while histamine was injected. It is possible, then, that the failure to maintain a rapid heart-rate in the normal dog involves a vagus reflex.

The continuous intravenous method of administration was selected, in order to conform as closely as possible to the procedure adopted in the experiments with acetylcholine. The effects of subcutaneous and intramuscular injections of histamine were, however, compared with those of intravenous injection. An amount of histamine acid phosphate equivalent to the average 90 minutes intravenous dose was injected subcutaneously. The flushing, vomiting and cardiac acceleration occurred as with the intravenous injection and the signs lasted for about 30 minutes longer. Following an intramuscular injection the same reactions occurred, rather more violently for the first 30 minutes, and passed off within an hour.

METHOD

The method was similar to that used in the experiments with acetylcholine. Preliminary determinations were made of normal rectal temperature, resting respiratory and heart-rates, heart-sounds, blood-pressure (Dameshek and Loman's method), electrocardiograms, blood-culture and body-weight.

Sterile histamine acid phosphate solution, 1/10,000 in normal saline, was injected from a sterile Mariotte bottle into a leg vein, at such a rate that the heart-rate was accelerated from the normal of 80 to 100 to a rate of 180 to 240 beats per minute. This heart-rate kept

remarkably constant as long as the dog remained quiet and the rate of injection was constant. No anæsthetic was used. The injection was maintained for 90 minutes daily, seven days in the week. The amount of histamine necessary to maintain the heart-rate at the desired level varied widely in the same dog from day to day, and was not proportional to body-weight, for a dog weighing 22 lbs. was found to require only about 20 per cent less than a dog weighing 44 lbs. The amount of histamine injected each day varied in one dog, *e.g.*, from 1.3 to 9 mg. of histamine base, and averaged for a 22 lb. dog, 3.4 mg. and for a 38 lb. dog, 38 mg.

The normal resting heart-rate, respiratory rate and rectal temperature were determined each day before the injection was started. The heart-sounds were noted and the rate was recorded frequently during the injection. The other preliminary observations were repeated weekly. A study of certain blood-constituents was also made and are reported separately (Lang and Ettinger).

RESULTS

Within 30 seconds of the start of injection there was an abrupt acceleration of the heart to a maximum which varied with the dog. Flushing of the face, mucous membranes, and skin areas which were not well covered with fur was observed. In one animal the upper lip became thickened from frequent congestion, and did not again resume its normal size. Vomiting frequently occurred and could be precipitated by increasing the rate of injection without increasing the heart-rate markedly. Salivation occurred, but was not so profuse as that caused by acetylcholine. A conditioned salivary response could be provoked by merely putting the animal on the table after the third injection. Bowel movements were rare.

The early injections caused discomfort in the dogs, but after the first week they lay quietly with excellent cooperation during the injection. One dog showed considerable delay in recovery from the effects of injection; for the first week he remained in mild shock for 20 to 30 minutes after each histamine injection was stopped. In other dogs the initial flushing partially faded each day during the last hour of the experiment, although the heart-rate remained high until the injection had been stopped. In these dogs, and in the more sensitive dog after the first week, the heart-rate fell almost to the normal within two minutes of the finish of the experiment.

Since the object of the experiment was to determine the organic changes induced, not by a fixed amount of histamine but by the physiological phenomena accompanying the induction of a fixed heart-rate by histamine, the drug was injected at a rate which, at the time, most easily produced this heart-rate. For the first

few days this was slightly in excess of the amount required later in the experiment; thereafter there was no suggestion of either tolerance or susceptibility, but the amount required varied considerably from day to day.

One of the dogs, (male, initial weight 58 lbs.) after 16 daily injections, contracted distemper. Up to that time he had gained weight and was in good health. He developed pneumonia, but the injections were continued daily for twenty days more. During that period his vomitus occasionally contained blood. He failed rapidly and died on the 39th day of the experiment, of pneumonia. Autopsy showed a pyloric ulcer, about 4 sq. cm. in size and a healed duodenal ulcer. (Ulcers produced by histamine were first reported by McIlroy in 1928). He had received a total of 263 mg. of histamine in 36 days an average of 7.3 mg. *per diem*.

The two other dogs (one, male, weight 38 lbs., the other, female, weight 22 lbs.), both with the right vago-sympathetic cut in the neck, were in good health throughout the experiment. They both gained weight. The female conceived and was delivered at full term, on the 72nd day of the experiment, of four normal puppies, which she was allowed to feed. Contrary to the observations of Spinelli¹¹ in the rabbit, parturition was not followed by a diminished susceptibility to histamine. She was injected with histamine for 191 consecutive days, except the 72nd, the day of the puppies' delivery. During that time she received 656 mg. of histamine, an average of 3.4 mg. daily. She had throughout this period no murmurs or other clinical evidence of impaired cardiovascular function. She was killed with chloroform on the 192nd day, and an autopsy done at once. All the thoracic and abdominal viscera looked healthy. There were no gastric or intestinal ulcers. Histological examination of the lungs, liver, spleen, pancreas, adrenal, kidney, and gastro-intestinal tract showed no degenerative changes in the arteries.

The third dog was given histamine daily over a period of 266 days. During that time he received 1,000 mg. histamine base, an average of 3.8 mg. daily. He gained weight and was in excellent health throughout, never showing any clinical signs of impaired cardiovascular function. He was killed by bleeding under ether on the 268th day. All the abdominal and thoracic viscera appeared healthy and none had arterial

degenerative changes revealed on histological examination. There were no gastric or intestinal ulcers.

EXAMINATION OF THE HEARTS

The hearts of all dogs were carefully examined at autopsy. No superficial changes were observed. Blocks were removed from the following places for fixation in formalin: a large piece through the anterior coronary artery, including the left descending branch, and cross-sections of the right and left ventricles and septum; longitudinal sections through the right and left myocardium; through right and left papillary muscles; through the interventricular septum; across the base of the left ventricle. Sections were stained with hæmatoxylin and with Millar's modification of Kull's stain, to show hyaline change (Millar⁷).

No degenerative changes were found in any of the specimens of any of the hearts.

CONCLUSION

Intravenous injection of a solution of histamine, given daily to dogs for periods up to 266

days, each injection lasting for 90 minutes, at a rate sufficient to accelerate the heart to two or three times the normal rate, does not cause any degenerative changes in the heart or its blood-vessels. It is unlikely, therefore, that the degenerative changes produced by Hall, Ettinger and Banting with acetylcholine administered in the same way were due solely to the combined effects of low blood-pressure and rapid heart-rate, with possible coronary arterial constriction.

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THE EFFECT OF REPEATED INJECTIONS OF HISTAMINE IN THE DOG

B. ON THE BLOOD

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THE changes in the blood produced by histamine injections have been reviewed and summarized by Best and McHenry.¹ These changes include a decrease in blood-chlorides and carbon dioxide combining power of plasma; an increase in blood non-protein nitrogen and sugar; and a general concentration of the blood, the result of an increase in the permeability of the vessel walls. As a result of this blood-concentration there is a marked increase in red blood-cell count and hæmoglobin, with a great decrease in blood-volume and leucocyte count. Although one would expect an accompanying increase in viscosity, Waud³ described a decrease.

Since the review of Best and McHenry, the

work which has been reported has not changed the conception held at that time, except that Raffin and Saradjichvili² consistently produced a condition of alkalosis by means of subcutaneous injections of histamine.

Since most of the reported work on histamine injections has been the result of acute or short-timed experiments, we have taken advantage of the opportunity to study the possible cumulative effects upon the chemical and cellular constituents of the blood in dogs which had been brought to a condition of mild histamine shock daily for many months (Ettinger, Hall and Lang, 1936).

EXPERIMENTAL WORK

The three dogs which were used in the experiment were given intravenous injections of physiological saline solution containing 0.1 mg. histamine acid phosphate per c.c. The injection, continued for 90 minutes each day, was given at a rate sufficient to maintain the heart-beat at

values obtained during the experimental period showed weekly variations, but were within normal limits.

In order to follow the blood changes during and immediately after one of the daily injections of histamine, blood-samples were taken just prior to the injection, 35 minutes after the

TABLE

	CO ₂ C.P. Vol. %			Chlorides mg. per c.c.			Non-protein nitrogen mg. per 100 c.c.			Sugar g. per 100 c.c.		
	Expt. 1	Expt. 2	Expt. 3	1	2	3	1	2	3	1	2	3
Before injection	52.9	51.5	48.8	5.97	4.51	4.83	43.2	39.0	34.8	0.120	0.125	0.108
35 minutes after beginning of injection	56.7	50.7	49.8	4.87	4.63	4.83	40.8	37.2	36.6	0.125	0.120	0.120
35 minutes after injection ..	58.5	50.7	50.7	4.67	4.73	5.07	39.0	41.4	36.0	0.125	0.116	0.125
4 hours after injection	49.3	47.2	44.1	5.03	4.71	5.13	43.8	40.8	34.8	0.120	0.125	0.108

about 200 beats per minute. The required amount of histamine varied widely in the same animal from day to day. The average daily injection was 0.3-0.4 mg. of histamine base per kilo of body weight.

The details of the injections are as follows:—

Dog 1.—Male, wt. 55 lbs., injected for 36 days; total histamine injected 263 mg.; average daily dose 7.3 mg.; maximal injection 13 mg.; minimal injection 3.5 mg.

Dog 2.—Female, wt. 22 lbs., injected for 191 days; total histamine injected 656 mg.; average daily dose 3.4 mg.; maximal injection 9 mg.; minimal injection 1.3 mg.

Dog 3.—Male, wt. 38 lbs., injected for 266 days; total histamine injected 1,000 mg.; average daily injection 3.8 mg.; maximal injection 9 mg.; minimal 2.6 mg.

Control samples of blood were drawn from the dogs before the commencement of the experiments, and then weekly throughout the experimental period. These routine samples were taken immediately preceding a daily injection of histamine. The following determinations were made on these blood-samples: carbon dioxide combining power of the plasma (Van Slyke and Cullen method); non-protein nitrogen of whole blood (micro-Nessler method); sugar content of whole blood (Shaffer-Hartmann method); chlorides of whole blood (Hanna modification of the McLean-Van Slyke method); viscosity of the blood (Hess); red and white blood-cell counts; hæmoglobin (Sahli-Leitz).

In the analysis of the control samples the carbon dioxide combining power values ranged from 43.8-50.1 volumes per cent; the chlorides from 4.73-5.49 mg. NaCl per c.c. of blood; the non-protein nitrogen from 36.3-39.6 mg. per 100 c.c. of blood; and the blood sugar from 0.093-0.116 grams glucose per 100 c.c. of blood. The

start of the injection, 35 minutes after the completion of the injection, and, finally, 4 hours later. This type of experiment was carried out on several different occasions. The results of such experiments (Nos. 1 and 3, Table I) show a definite though small increase in the carbon dioxide combining power during the injection of histamine. Considering that about 100 c.c. of fluid were injected during the 90 minutes, and allowing for this dilution of the blood, the above values would tend to be increased even further. Four hours after the injection the values of the carbon dioxide combining power in all experiments had decreased to a level below the pre-injection value. These values were again normal before the next daily injection. There were no significant changes in the other constituents noted.

CONCLUSIONS

Mild histamine shock, induced for 90 minutes daily in the dog for periods up to 266 days by daily intravenous injections of histamine, did not cause any cumulative change in the red or white blood-cell count, the blood-viscosity nor in the blood-chlorides, non-protein nitrogen, sugar or carbon dioxide combining power. The values of the carbon dioxide combining power increased during any one daily injection of histamine, decreased to a sub-normal level within 4 hours after the injection, and returned to normal within 24 hours.

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Case Reports

AN UNUSUAL CASE OF OBSTRUCTIVE JAUNDICE AND SEPTICÆMIA*

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The end-results of obstructive jaundice of several weeks' standing in men who have reached 65 years are more often unhappy than comforting, and to have complete recovery in a case of jaundice with enlarged liver, complicated by hæmorrhage, double parotiditis, and multiple abscess formation, must be unusual to a degree. For this reason, we are tempted to report the following clinical history.

Capt. E., aged 65, pensioned for enlargement of the heart with electrocardiographic changes suggesting severe myocardial abnormality, became jaundiced early in July, 1934, without any preceding hint of gastrointestinal disease. He had usually enjoyed fair health, with the exception of one or two attacks in the past which suggested appendicitis. The jaundice deepened; he began to complain of a great deal of itching; there was a slight temperature of 99.2°; and his weight began to go down persistently; while his blood pressure, which had been in the neighbourhood of 170/120, began also to fall slowly. At the end of a month, however, while under observation outside the hospital, all that could be noted was that he was deeply jaundiced, that his liver was enlarged though quite smooth, that the urine was very high-coloured and contained bile, and that the fæces were practically clay-coloured. The suspicion was that, in a man of his age with painless obstructive jaundice, some malignant growth was pressing upon the bile duct. Neither gall-bladder nor spleen could be felt.

In the middle of August severe hæmorrhage from the nasal mucous membranes occurred. The hæmorrhage persisted for many hours, and it was deemed wise to bring the patient into the hospital and to pack the nasal passages, pending an opportunity to make further investigation. On August 20th, the hospital note states "that the jaundice is deep, that the bleeding had stopped after twenty-four hours, that the temperature was running between 99 and 100°, that the itching was extreme, and that there were very evident signs of obstruction of the common bile duct in the presence of bile-colouring matters in the urine and their complete absence in the bowel movements." No abrasions had been seen in the nose, nor had the source of the bleeding been localized to any one spot.

The blood examinations made at the time of admission indicated that there had been considerable loss of blood, with hæmoglobin, 60 per cent; red blood cells, 3,500,000; white cells, 10,000. There was nothing in the stained smear nor in the differential count in the least suggestive, save the evident increase of the white cells. The platelets were numerous. Both bleeding and clotting time were well within normal range. There was no increase in the fragility of the red cells. The serum was very distinctly bile-stained. No attempts were made at this time to put the desperately ill patient through a barium series examination or through the process of

photographing the gall-bladder after the injection of iodeikon, it being felt that the liver should be spared further damage. Calcium was freely administered, and as the oozing of the blood began to slacken after forty-eight hours, leaving the patient by no means very anæmic, transfusions were not suggested. The packing was removed from the nose after seventy-two hours by Dr. Pentecost, who at the time could see no evident lesions in the nasal mucous membranes.

Five days after the nasal packing was removed acute painful swelling of the left parotid gland developed. The temperature rose to 101°, the jaundice deepened, the liver seemed larger, and the patient was desperately ill. A day later the right parotid became sore, swollen and tender, and the white blood count was found to be 17,000 per c.mm. With the double parotid involvement, the rising temperature, the deepening jaundice, and some mental confusion, the outlook seemed very dubious. Only the simplest tests of liver function were thought to be permissible and the van den Bergh was found to read, direct, double plus,—indirect, 16 units. The galactose test of liver function showed some distinct impairment. The temperature now reached 102 and 103°, but the parotid swellings had begun to subside, and it was found that this higher range of temperature was due to an erysipelas which was developing over the right side of the face and ear. This persisted for some days, though at the end of August it was noted that the jaundice seemed to be lessening, that the liver, though swollen, was not so large as it had been formerly, and that the general signs of toxæmia were distinctly less. Coincidentally with the erysipelas, the right submaxillary gland became swollen, and this persisted almost unaltered for a month, at which time it joined the long procession of suppurations to be described, and had in turn to be opened.

At the end of the first week in September the patient began to complain of some pain in the left lower part of his abdomen, more or less in the situation in which painful swellings associated with diverticulitis might appear, and for a matter of two weeks the meaning of a slowly developing mass in this region was most puzzling. This mass could not be felt through the rectum, nor could anything be seen with the sigmoidoscope. Palpation gave the suggestion that it was more intimately connected with the muscles of the abdomen than with the abdominal contents. Tenderness over the irregular swelling became pronounced. On September 9th, the patient had a severe chill, after which his temperature reached 104° and his white count mounted to 40,000 per c.mm. There were no evident signs of pointing in the tumefaction, now as large as a man's hand and extremely tender. There was no swelling in the flank, and the impression was slowly gained that the mass was of an inflammatory nature and situated superficially. In the absence of pointing or softening surgical consultants did not urge incision.

While debating the nature of the inflammation on the left front abdomen, the attending physicians were confronted with yet another pyæmic manifestation. The patient began to complain of pain under the right costal margin in the axilla and back, and it became evident that a painful swelling was developing in the right perirenal area. The patient, nevertheless, seemed to have begun to brighten, the jaundice was less intense, the bowel movements were beginning to show colour, and numerous blood cultures failed to show any growth. Both parotids had subsided without suppuration, though the swelling of the right submaxillary gland still remained. By September 18th, ten days from its appearance, the mass in the left lower front showed signs of pointing and was incised, and a large amount of pus was evacuated from which a short-chain streptococcus was obtained. The white count now dropped to 18,500;

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the urine, which had been heavily albuminous and full of casts and pus, cleared quickly.

Four days later it became necessary to make the large swelling which had appeared in the right perirenal area, a pint of pus, heavily infected with streptococci, was found and released, and after this second operation the temperature, which had been elevated for seven weeks, dropped slowly to normal. Both operations were successfully done under local anesthesia. It had been hoped that the perirenal abscess might represent the end of the suppurative process. One week later, however, the glands in the posterior triangle on the left side of the neck began to swell greatly and two days later, on October 4th, there appeared incrustations on the skin. It was noted at this time that the right submaxillary gland was still swollen and sore, and in fact it required opening at this time. The pus from the gland and from the glands on the left side of the neck contained again short chain streptococci. Blood cultures, however, remained persistently negative, and the rate of the long history of infection with suppuration, the blood count never dropped below ten per cent hemoglobin and 3,500,000 red cells.

After the opening of the submaxillary and cervical glands all signs of jaundice quickly disappeared, the patient's general condition began to improve, and from this time on no setbacks were experienced. Reporting for examination a year later, the patient was at work and in excellent shape. Nothing had been found in the series or in a careful examination of the gall-bladder and bile ducts.*

In considering this case, particularly interesting from the clinical side and from the various opinions expressed as to the cause of the jaundice and subsequent pyæmic manifestations, a few words might be added. It is comforting to realize that not all cases of deepening jaundice associated with obstruction of the bile duct and large liver, even if occurring in elderly men, are due to malignant disease. Whether the bile duct had been closed by stone, by inflammation extending, perhaps, from a duodenal ulcer, or by some external pressure cannot be said. Either of the first two conditions might clear up without leaving a trace, but it would be difficult to visualize any form of external pressure upon the bile duct which might develop without symptoms and disappear during the course of a long illness. All possible portals of entry through which an infection might enter the body, teeth, tonsils, lower bowel, bladder, kidneys, prostate, sinuses were carefully examined. It was impossible to undertake any special examination of the stomach, duodenum or gall-bladder while the acute pyæmia was progressing. Pancreatic disease was frequently discussed. It was sug-

gested that the packing of the upper air passages during the acute hemorrhage may have caused lacerations sufficient to allow the entry of infection, though one would suggest in this connection that some glands, other than the parotid, would show the first response. It is well recognized that in operations upon the mouth an acute parotitis may develop, but it must be unusual to see these glands involved following the packing of the nasal passages. An embolic origin would seem the more likely.

In the patient's deeply jaundiced condition a low resistance to infection would be a likely association, and a general septicæmia with a fatal outcome was feared when first the parotids became inflamed, and next an erysipelas appeared over the face and right ear. In spite of all fears, however, the patient showed the ability to localize his infections, and the large abscesses in the abdominal wall on the left side, in the peri-renal tissues on the right side, in the glands of the posterior triangle and the submaxillary area, came to a head, were drained, and cleared up completely. The localization in the muscles on the left side of the abdomen brought forth the suggestion that an acute degeneration of the muscle, such as has often been described in typhoid fever or in infectious jaundice, may have determined the localization of suppuration in the muscle tissue. The negative results of all blood cultures would seem to indicate that the blood itself contained antibodies sufficient to prevent the development of a general septicæmia, while the breaking down of tissue in so many other portions of the body might suggest that impaired circulation and a lowering of local immunity contributed to the abscess formation. In the early part of the patient's illness it was but natural that, in addition to obstruction of the bile ducts, a development of some such condition as acute yellow atrophy, progressive cirrhosis and hepatitis should be considered. All the findings, however, pointed to an obstructive jaundice, and the smooth large liver, with absence of leucin and tyrosin in the urine were strongly against inflammatory and degenerative hepatic conditions.

It is of interest to realize that a myocardium of which electrocardiographic record had said "indications of serious myocardial disease" could weather the storms to which it was subjected, and in this connection it might be said that the persistence of a good pulse volume and

* March, 1936. Reappearance of obstructive jaundice with enlargement of the liver. Exploratory operation: small primary carcinoma of the common bile duct. Removal. Improvement. In this case one must entertain the possibility that a carcinoma existed two years ago and that the high fever and septicæmia was responsible for a recession of the growth and the disappearance of symptoms. (July, 1936). N.B.G.

a fair appetite throughout the patient's illness were two points which always lent hope to the idea that he might come safely through his serious infection. The lessening of the jaundice following the bleeding and the infectious was an interesting coincidence, though the bleeding had never been sufficient to produce a very intense anaemia. It is probable that some simple form of obstruction in the common duct relieved itself as the illness went on, for the clearing-up of a persistent jaundice immediately subsequent to a gastro-intestinal hæmorrhage has been frequently observed, even though the method of action in this occurrence has remained obscure.

During the many weeks of Capt. E.'s illness a line of conduct mostly devoted to careful observation of symptoms and physical signs was largely followed. After the first week the further employment of calcium did not seem indicated. Outside consultants suggested intramuscular injections of liver extract as a possible treatment for the acute yellow atrophy which to their minds was presumed to exist. Such treatment has been advocated in cases of hæmolytic jaundice with liver and spleen enlargement, but without, so far as we can see, any convincing results. The large, smooth liver, the very positive signs of obstruction to the bile duct, the failure to find leucin or tyrosine crystals in the urine, had always, to our minds, spoken against the existence of an acute hepatitis with atrophy. Any toxic symptoms and febrile reaction we attributed more to the long-standing infection than to any intoxication resulting from acute liver degeneration. To combat the exhaustion consequent upon the development of the many suppurations transfusions were resorted to.

From the prognostic side there were opinions many and various. After the development of the parotid inflammations and the spreading erysipelas, at which time the diagnosis of acute yellow atrophy was made, ten days of life seemed a generous allowance, yet to those who had followed the patient's illness from the beginning, the clearness of intellect (save for two days during the spread of the erysipelas), the moist tongue, the good heart sounds, and the persistently negative blood cultures gave always much encouragement.

In concluding, we would thank the laboratory for innumerable tests and examinations most carefully and at all times performed, and the surgical consultant, Dr. Shenstone, for valuable advice.

A CLINICAL CASE OF HYPER-VENTILATION TETANY*

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AND

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The number of published cases of tetany associated with hyperventilation appears to be so small that every new case should be recorded. The literature has been reviewed by Monteith and Cameron¹ and by McCance.² The outstanding features in every case are marked lung hyperventilation (deep and rapid breathing), normal or very slightly increased serum calcium, and definite tetanic manifestations. Various causes lead to hyperventilation and the precise cause is often obscure.

The present case is one of a pupil nurse, Miss G., aged 20, in her first year of training. She said that she had felt rather unwell for a week prior to the onset, and that she had had a sore throat. She did not report sick until 6 a.m. and awoke, shortly before that, coughing. She said that she was unable to get some sputum past the region of her larynx and felt as though she was going to suffocate. She soon was breathing rapidly and deeply in an endeavour to overcome this sensation. When seen about an hour after the onset she was still breathing very rapidly (about 60 times a minute) and deeply. The respirations were now accompanied by a very loud inspiratory stridor. Her colour was good, and her heart and lungs appeared to be normal. Her pharynx was deeply congested. At that time there was no evidence of muscular spasm, and the only objective finding in her central nervous system was markedly hyperactive knee jerks. Her condition was not recognized and she was given morphine hypodermically and gradually quietened down. Further examination now showed a little greyish exudate in the right tonsillar fossa. The whole of the larynx was deeply congested, and a little greyish exudate was seen in the right arytenoid fossa.

Within an hour and a half she was again breathing very rapidly and noisily. She was propped up in bed and seemed to be having very severe respiratory distress, using all her respiratory muscles. Her colour remained good so that laryngeal obstruction could be ruled out. Very soon afterwards she again developed the respiratory stridor noted before and she became very restless and distressed. A half an hour later it was noted that her hands had become spastic and had assumed the characteristic "obstetrical position of the hands." Her legs stiffened and the feet were markedly plantar flexed. The stridor continued to be very loud and the respiratory rate continued about 60 per minute. When a tourniquet was applied to her arm for the purpose of obtaining a sample of blood her hand assumed a most characteristic tetanic spasm, i.e., Trousseau's sign was positive. Chvostek's sign could not be elicited satisfactorily.

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The serum calcium was found to be 10.7 mg. per 100 c.c., and the urine was markedly alkaline. She vomited several times after an attempt to give her hydrochloric acid by mouth. A short time later she quietened down under the influence of morphia and the tetanic manifestations disappeared.

During the afternoon she was visited by her mother and some friends, and in a few moments she started to become very restless and recommenced her rapid breathing. The stridor reappeared and it was thought that she would again develop a full attack of tetany. However her condition was carefully explained to her, and after considerable coaxing and persuasion she voluntarily, though slowly, decreased the rate and volume of her respirations, and the attack was aborted without any medication. During the succeeding evening and night she started to increase her respirations on several occasions, but in each instance was persuaded to stop. She was kept in bed for several days and had no recurrences. The inflammatory condition of the pharynx and larynx rapidly cleared up.

No cause for her hyperventilation could be found other than the fear of suffocation which resulted from an attempt, when half awake, to clear her throat. She was found to be somewhat unstable emotionally, and it appeared that she had been told that she had a damaged heart

when she was twelve years old. She had worked on a medical ward, where no doubt she saw many cases of respiratory difficulty in advanced cardiac cases; further, she had worked for a brief period on a nose and throat ward where she had the opportunity of seeing some cases with tracheotomies following laryngeal obstruction. Her record as a nurse was good, and she said she liked her work.

It is interesting to note in this case the success of persuasion in preventing further attacks of tetany which were undoubtedly due to an hysterical hyperventilation. This appears to be the first case reported in which symptoms of laryngeal spasm, as evidenced by inspiratory stridor, are recorded in hyperventilation tetany.

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Clinical and Laboratory Notes

SEEKING TUBERCULOSIS WITH THE AID OF A MICROSCOPE

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The following is a report of the examination of sputum obtained from 44 Cree and 16 Chipewyan Indians. The Crees were located on their Reserve at Willow Lake and the Chipewyans about Lake Athabaska. The Indians were chosen because they had some slight symptom, such as persistent cough, or because sputum could be obtained. The individuals were carrying on with their various occupations, which were, chiefly, fishing in summer and trapping in winter—not in a single instance was one bedridden. This information was obtained in Northern Alberta as an interesting side line whilst assisting in the research being carried on by the Connaught Laboratories.

The data gathered indicate a greater percentage of positive sputum between the ages of fifteen to twenty-five. (All the positive sputums in Group 25—29 years were as age 25.) A greater number of children at the age of five were found to have positive sputum than would probably be found in white children living under the same environmental conditions; this probably would be due to prevalent infection.

CREES

Age Groups	50%		75%		100%		Total	
	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
Under 5 years	0	1	0	2	0	1	0	4
5 - 14 years	0	0	1	3	1	3	2	6
15 - 19 "	0	0	0	2	0	2	0	4
20 - 24 "	0	0	2	0	0	2	2	2
25 - 29 "	0	0	2	1	3	0	5	1
30 - 39 "	0	0	0	1	1	1	1	2
40 - 49 "	1	0	0	2	1	1	2	3
50 and over	0	0	0	4	2	4	2	8

CHIPLEWYANS

Age Groups	50%		75%		100%		Total	
	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
Under 5 years	0	2	0	2	0	0	0	4
5 - 14 years	0	0	2	1	0	0	2	1
15 - 19 "	0	0	0	1	0	0	0	1
20 - 24 "	0	0	1	2	1	0	2	2
25 - 29 "	0	0	1	0	0	0	1	0
30 - 39 "	0	1	0	0	0	1	0	2
40 - 49 "	0	1	0	0	0	0	0	1
50 and over	0	0	0	0	0	0	0	0

N.B.—The three divisions, 50%, 75% and 100%, refer to the amount of Indian strain in each individual.

In this survey only sputums were examined, no other examinations were carried, doubtful sputums being checked two and three times for accuracy. Yet by this simple method many persons were proved to be tuberculous.

Editorial

THE VICTORIA MEETING

THE Victoria meeting of the Association was undoubtedly an outstanding success. The excellent innovation of the last few years, following the example of the British Medical Association, whereby the social side was not sacrificed to the scientific side, as it used to be, deserves a word of commendation. Not that the scientific contributions were neglected, for, indeed, the program of the various sessions was most interesting and occupied from nine to five of three days, but the work of the various sessions was not allowed to clash with the general meetings. When one reflects that the majority of the men attending were general practitioners and interested in things of a general as well as of a special nature, one can only applaud this arrangement. If a man, for instance, desired to hear a paper in the surgical section on Wednesday afternoon, he did not need to give up an address in a general session, and contrariwise; although, of course, he might have to sacrifice a paper in one of the other special sections. The programs of all sections strike one as interesting and well selected. In the general session there were papers by distinguished men—our own Banting and Best and Collip, and Dr. Verne Hunt from Los Angeles; and in the work of the sections valuable papers were read by leaders of the profession in Canada, and from the northwestern states of the Union. All parts of Canada were represented, but naturally the majority of the contributions came from the middle-west and the west. Our French confrères were represented by Major Petitclerc, of Quebec, who wrote of the treatment of wounds in French hospitals. The Maritime Provinces alone appear not

to have anybody on the program; but it is a "far cry from Loch Awe"!

A feature of the annual general meeting on Wednesday evening, at the Empress Hotel, was the presentation of the Frederic Newton Gisborne Starr medals to Sir Frederick Banting, Dr. Charles Best, and Dr. J. B. Collip, which excited great enthusiasm. The medals were presented by Mrs. F. N. G. Starr, and she perhaps received an even more hearty ovation than the recipients. It was the more fitting and the more pleasurable that she, who is perhaps the most widely known and the most universally admired of all the silent partners of the profession, should herself make the presentations, in that she nearly always accompanied Dr. Starr to these meetings.

Victoria is undoubtedly the most delightful place in all Canada in which to hold a summer meeting. Old Sol was at his best and Jupiter Pluvius came not near, and the temperature was moderate, but that is what Victorians count upon the year round! The people of the town outdid themselves in hospitality. Nowhere else, one must believe, can one find such lovely gardens, such magnificent lawns, and such a profusion of flowers and trees. The thanks of the Association are particularly due to the President and Mrs. Robertson, Lady Barnard, Mr. and Mrs. R. P. Butchart, Mr. and Mrs. James Dunsmuir, Mrs. Norman Yarrow, and Mrs. J. W. Spencer, who all received the members at garden-parties. The reception given by the Lieutenant-Governor, on Friday afternoon, at Government House, was a memorable occasion. This meeting will live long in the memory of our members. E. W. A.

MODERN HISTOLOGY IN THE MEDICAL CURRICULUM AND ITS
BEARING ON PATHOLOGY

THE great advances made in histology during the last few decades have brought it to the position of a major subject in the curriculum. From a mere exercise in morphological description, often without practical meaning, it has become "as 'twere, the mirror" held up to Nature, in which is reflected all of our present knowledge of the protoplasmic substrate—the vital fabric in which the processes of life take place. These reflections are not only exceedingly numerous but of most varied character, for in the multitude of research workers who have given rise to them we find large groups of pathologists, physiologists, biologists, clinicians and others who have combined with the professional histologists to bring to bear upon the problems a rich assortment of technique and points of view. But the very number and diversity of the fragments would have made the composite picture incomprehensible had it not been that the parts have been put together by the aid of the physiological *motif*, and the mirror now presents to us the finer details of an intelligible unity—the living human body. That microscopic structure is best interpreted in terms of function is one of the two great dominating principles of modern histology; and the other is that protoplasm is best studied in *living cells* in a suitable setting. The application of these vital guides has led to the all-important emphasis upon the dynamic nature of protoplasm rather than the static, as suggested by fixed material.

Dynamic protoplasm has been demonstrated by a number of ingenious methods. The thin tail fins of living tadpoles and minnows, conveniently held before the high-power lenses of compound microscopes, have shown us myelin actually being laid down around the axis cylinders of growing nerves; the hollowing amoeboid buds of tiny blood vessels and lymphatics pushing themselves through their own nutrient body fluids, and many other glimpses of fluctuant, law-controlled protoplasm. Cleverly devised collodion chambers inserted into holes punched through the ears of rabbits have become show-windows behind whose panes is dis-

played for months or longer an almost infinite variety of cellular phenomena, of which we shall mention only the functional widening and narrowing movements of the arterioles, the form and behaviour of arterio-venous anastomoses, and the contractile nature of the capillary wall.

The cells of tissue cultures, spread like "veils of thinnest lawn" for direct and continuous observation over long periods, prove that chromosomes and organoids such as the centrosomes and mitochondria are realities whose functional form-changes may be followed. Here have been mirrored vital processes, like the contractions of individual muscle fibres, untended by nerves, or the intake of bacteria and other particulate matter in phagocytosis. Nerve fibres have been seen to grow out from cells, thus settling the question of their origin finally. Cultures of cancer tissue have impressed upon us not so much the differences which these cells present when compared with normal cells as the similarities; and have thus forced us to realize something of the profundity of the cancer problem, which is as deep as the mystery of life itself. Motion pictures of cells thus growing *in vitro*, when taken at relatively long intervals and shown at the usual rate, give a dramatic exhibition of movements of cells and their parts that would be otherwise unappreciable. Even the dividing ova of higher mammals have been photographed thus, so presenting segmentation in a new light. Microdissection has made it possible to separate and examine the parts of the cell, and we have learned, for instance, that the nuclear membrane is tough and elastic, and that the fibrils of the amphister may be pulled upon and made to move the attached chromosomes. Micro-surgery has been used, and experiments enlisting the most recent discoveries of chemistry and physics performed. We have been given reassurance as to the actuality of formations which have in the past been dismissed as artefacts. No longer may the protoplasm be put off as a mere "colloid", useful though that term may be. We realize that the cell is a universe in itself, and this conception is

made all the more evident in the light of recent research in physics on the ultimate subdivisions of matter. The parts of the cell which we can move about and operate upon are really very huge masses when considered in the light of the theory of relativity.

Vital staining has increased the visibility of certain granules and vacuoles of cells, and has discovered for us the far-flung ranks of the macrophages which make up the reticulo-endothelial system. Supravital staining has brought from invisibility into strong relief the fine tendrils of nerve endings. And while all this has been going on, the older techniques have been improved and enriched to an unrecognizable degree. Only an instance or two from this great realm can be mentioned. Cells of different types have been identified in the previously apparently homogeneous islets of the pancreas, hypophysis and other organs, and definite functions have been, or will be, assigned to these. Special silver techniques have not only disclosed the different forms of neuroglia cells, but have proved their complicity in certain brain tumours, and have even aided prognosis in such cases.

Histology has thus developed, within a generation, into a medical science of the first magnitude, and has come to occupy a central position in the group of pre-clinical studies. It includes much physiology, but what branch of medicine does not? It is also intimately integrated with embryology, gross anatomy, biochemistry, pharmacology and all of the clinical subdivisions. Its relation with pathology is particularly close; it is an immediate prerequisite to this science. Indeed, in the great development of histology the borderland which formerly separated it from pathology has become obliterated, so that the one now grades directly into the other. Thus it has come to pass that the histologist, in analyzing the bodily fabric for his students, has the opportunity, indeed obligation, to refer to departures from the normal, and to give to the students previews into the pathological field, thus increasing their interest, aiding their memory, and imparting an impetus which will help the pathologist by reducing the amount of his preparatory work. For instance, the histologist can point out that normality is a relative term, and that the picture of the normal

varies with age and functional state. The arterial wall, particularly that of the elastic type, when viewed in the entire age-range of a normal life is seen to present an ever-increasing deterioration, each stage of which is quite normal for that age. Here, obviously, histology joins hands with pathology, for the pathologist, building upon such information, is able to decide whether the age degeneration in any given specimen which he is called upon to examine is less than, equal to, or greater than what is to be expected for that age. The same remarks apply to the myocardium, renal cortex, thymus, spleen, uterus, bone and other tissues. There is still need for more accurate age standardization of the normal in the different tissues at all points of the life range, but the histologist should present these standards for human tissues as exactly as his present knowledge will permit.

Cellular changes due to function should be well taught to afford a firm basis for pathological diagnosis. These changes may turn in a cycle of relatively short duration, as in the externally secreting glands, where variations in such items as the secretion granule collections should be pointed out. Equally important, but less well known, because of more recent discovery, are phenomena like the diurnal periodicity in the liver parenchyma which Forsgren has described. What was formerly thought to be some form of degeneration is now shown to indicate but the normal accumulation of water and glycogen in the cytoplasm. Knowledge of the functional variation in the liver cells may be directly used by the pathologist in interpreting his sections. Even more striking is the functional change presented by the uterus during the period from puberty to the menopause. Here we have a regularly recurring cycle involving periodic building up and breaking down of the superficial part of the endometrium. No wise pathologist now diagnoses uterine scrapings from this period of life without first knowing the stage of the menstrual cycle that is being dealt with. It may be added that histological research, by making clear these changes in the menstrual cycle, has done much to stop the former unwarranted removal by curettement of what really was normal endometrium in the premenstrual stage, under the mistaken as-

sumption that it was in the condition of "endometritis". Now, too, it has been discovered that the mammary gland undergoes a definite, though less obvious, evolutionary and involutionary cycle coincidental with that of the endometrium.

Growth is at bottom an histological phenomenon, and it is the duty of the histologist to instruct the student in its various manifestations and laws. He is then able to contrast normal controlled growth with the abnormal and uncontrolled proliferation of tumours, so driving home the truths of the former, while awakening in the student a desire to know more about neoplasms. The student becomes "cancer-conscious", and begins at once to build up his knowledge of malignancy upon a firm foundation. The histologist can go farther and point out the preferred sites of tumours—while considering the gastro-intestinal tract, for instance, which is the site of one-half of all tumours, and where they tend to be segregated, in the cardia, pylorus and rectum. It is then but a step to the discussion of the hereditary factor in neoplasms, for there is strong evidence that tumours of definite type, as polypoid growths of the rectum, *tend to recur in the same region, at about the same time, in near relatives*. No longer may the clinician dismiss the conception of the hereditary nature of cancer with the airy pronouncement "It just doesn't hold water". When we reflect that cancer tissue develops out of the body's own cells, which are undeniably controlled by the laws of heredity, it is difficult to understand the opposition to the view that cancer is inherited, particularly now that the mass of recent evidence favouring this view is so large and convincing. When this is said, the rôle of irritation is freely admitted: indeed heredity and irritation work together to produce cancer, and where heredity predisposes, the threshold for irritation is lowered. We are making more and more use of the fourth dimension, that of time, in all histological work, and generations of cells are now viewed as a "continuum", and when this method of thinking is used logically in dealing with the cancer problem, the hereditary theory of origin comes as a matter of course. It is important, however, in touching on such points in histology, to avoid infringing on the

ground of the pathologist, and to present them as cellular phenomena, immediately related to the normal. The histologist should, above all, refrain from imparting one-sided views which may become crystallized into "heresies", and impede rather than aid.

Since the laws of heredity reside in the cells it is plain that it is the duty of the histologist to point out their *modus operandi* in all the cells and tissues with which he deals, for all of them have their hereditary features, expressed or latent. In this way a close integration with pathology may be accomplished. In doing this the teaching work is very much increased, but the effect in medical education is of such importance that it must be done. Thus, in dealing with the blood-forming tissues, the correlations with such diseases as pernicious anæmia and the leukæmias may be touched upon and their hereditary phenomena mentioned. The same may be done for premature degenerations of the cardio-vascular system, for the islets of Langerhans in relation to diabetes, the central nervous system with its abiotrophies, and many other tissues. All of this basis of heredity lies in the tissues, and its exposition lays in the mind of the student a foundation upon which may be reared the superstructure of medical hereditary science in the later clinical years.

Such correlations could be multiplied almost indefinitely. The need for constantly making practical applications of histological truths is specially pressing, now that the emphasis on the microscopic side of pathology is so much stronger. No medical school can rise higher than the level of its pathological teaching, and this is, more than ever before, dependent upon a thorough grounding in modern histology. Pathology is the hinge around which the entire medical course turns, and anything that contributes to its effectiveness adds just that much more to the value of the medical course as a whole.

The university should provide adequately for modern histology by furnishing an ample budget, space and equipment, time apportionment, and voice in the school administration. As to the curriculum, it is well that gross anatomy and embryology should precede histology, and that pathology should come immediately after it, so that one passes directly into the other. Human

material should be used in teaching, of course. Proper integration with physiology is essential. Due prominence in examinations should be accorded by universities and licensing bodies. Why should not the Royal College of Physicians and Surgeons of Canada take the lead by including a paper in modern histology under the supervision of a specialist in this field? Canadian medical institutions should develop their individuality and refrain from copying too sedulously the British mode, particularly in respect of features which even our British friends are trying to discard. Histological teachers should be medically trained, and recognized internationally for their scientific achievement. It is of the utmost importance that the staff be ample, so that all will have an abundance of time for research. Histological research should be promoted in every way. It is high time that our leading universities de-

veloped Histological Institutes equal to, or better than, those of Europe and the United States. The provision for histological activity in Canadian Schools of Medicine today is inadequate, to say the least. There is too much retardation by the dead hand of yesterday. In no field of medicine are the opportunities for useful research better, in both "pure science" and "practical" aspects, than in modern histology. There should be very much more opportunity for research students to undergo training, for without the preparation of our youth the forecast is gloomy. Research is the leaven of the university, and without it the loaf must be sodden and dead. The reflection in our "mirror of Nature" is even yet imperfect; we see "as in a glass darkly" in many ways, but are confident that time and research will make the picture increasingly clear and complete.

C. C. MACKLIN

Editorial Comments

Canadian Experience with BCG Vaccine

In 1925 the National Research Council of Canada appointed a sub-committee on tuberculosis research. One of the problems to be studied was the value of BCG in the prevention of the disease. Up to this date quite contrary opinions were being expressed on this subject, and among English-speaking workers, at least, a decidedly skeptical attitude was being maintained. It was felt by most of these that Calmette's opinion was too optimistic, and that his conclusions were statistically unsound. Sufficient time has elapsed since then to allow us to appraise more accurately the work of the many investigators of the subject. The only studies made in Canada on the preventive use of BCG are those undertaken by the University of Montreal, under the direction of Prof. J. A. Baudouin, as part of the program mapped out by the sub-committee mentioned. These investigations have been carried on continuously since 1925 and the results will be received with interest. We commend to our readers an article by Professor Baudouin, entitled "Vaccination against tuberculosis", which gives much food for thought.¹

During eight years, from June, 1926, to the end of 1934, in the City of Montreal, BCG was given to 5,126 children. Of these, 582 were

exposed in their family circles to open or presumably closed tuberculosis, the open cases numbering 249. There were 971 children living under the same conditions, 500 of them exposed to open tuberculosis, who were not given BCG; these served as controls. All of the 1,553 children were carefully observed and studied, and, to eliminate extraneous factors, no account was taken of those who died during the first month of their existence. Between the ages of one month and seven years the mortality from all causes was 10.3 per cent in the case of those inoculated and 18.7 per cent in the controls; the deaths from tuberculosis among the inoculated amounted to 2.1 per cent, and among the controls, 7 per cent. A study of the children of the same age-period living in contact with open cases of tuberculosis showed that the morbidity from tuberculosis was 1.7 per cent in those inoculated with BCG and 6.2 per cent in the controls. Professor Baudouin, therefore, is a thorough believer in the efficacy of BCG as a preventive of tuberculosis, and concludes his paper with this sentence—"The findings tend to show more and more conclusively with each succeeding year of observation that BCG vaccination against tuberculosis must be included as part of a complete campaign for the control of this disease."

The research work on BCG in Montreal has for some years been under the direction of Dr. Armand Frappier, Professor of Bacteriology in the University of Montreal. He has contributed

1. BAUDOUIN, J. A.: Vaccination against tuberculosis, *Canad. Pub. Health J.*, 1936, 27: 20.

a useful summary² of the various studies on BCG which have been undertaken in various countries in connection with the Calmette procedure and details some of his own observations on the pathogenicity of the Calmette strain. In regard to the pathogenicity question he does not think it necessary to refute the contentions of Petroff, Watson, and Hytura, the doughtiest opponents of Calmette, in view of the facts that Petroff is now silent on the matter, that Watson's last publication admits the gradual attenuation of the strain which he had at first found to be virulent, and that Hytura now asserts the perfect harmlessness of BCG and recommends its use. Dr. Frappier cites the special technical Conference organized by the League of Nations in 1928, the International Conference at Oslo on Tuberculosis in 1930, the Commission of the Ukraine and the Academy of Medicine in 1931 as in accord as to the harmlessness of BCG. For him, BCG is a "fixed" virus, harmless and irreversible. He also thinks that BCG will complete the victory against tuberculosis.

That BCG is harmless seems now to be generally admitted, although vaccination by its means has not yet proved popular on this side the water, being, so far as we are informed, practised on an extensive scale only in Montreal, and the method has had no following in Great Britain. Speaking at the twenty-first annual conference of the National Association for the Prevention of Tuberculosis, held at Southport, England, in 1935, Rist, of Paris, stated that BCG vaccination was not dangerous, and others agreed with him, but there is still some debate as to the degree of immunity produced. Rist quoted Walgren, of Sweden, to the effect that vaccination with BCG could protect previously uninfected children against virulent infection, but that the immunity produced was probably neither lasting nor absolute. Naeslund³ concludes that BCG is harmless and, according to his own researches, has proved beneficial, but does not argue that any convincing case has been made out for specific immunization by BCG against tuberculosis. His investigations are still progressing.

A.G.N.

2. FRAPPIER, A.: Le vaccin antituberculeux BCG, *Rev. Trimestrielle Canadienne*, Sept., 1935.

3. NAESLUND, C.: Experiences with Calmette-Guérin vaccination in Norbotten, *Nord. Med. Tidskrift.*, 1935, 9: 616.

Suggestions for a Health Program in Quebec

We believe that the fullest prominence should be given to all suggestions which look toward the solution of our public health problems. As our readers know, we have been continually striving in these pages to present the phases of these problems as they develop, and the various attempts made to deal with them. The

recent legislation in British Columbia is the most definite plan yet put into force by a Provincial Government, although as it stands it does not satisfy the minds of our profession. In Ontario, also, plans have been formulated along various lines to deal with this ever-pressing problem.

In the present number we publish certain proposals made as the result of studies made by a group in Montreal, which we are sure will be read with great interest by all concerned. There has as yet been no official recognition by the Quebec Provincial Government of the claims of medical men in caring for the unemployed. In isolated instances, as in Montreal, some provision has been made for the satisfaction of these claims, but only to a minimum extent and only after representations whose repetition has been a humiliation. What is proposed now by this study group goes much farther. The rights of the medical men to payment for their work are insisted on, but, just as important, the rights of the unemployed to claim this attention and to be assured of it are kept carefully in the forefront. It is well said that "a man should not lose his rights as a citizen because he loses his job." This study also presents facts and analyses of great and perturbing interest, such for instance as the statement that the unemployable on relief in Quebec form 48.71 per cent of the total unemployable in the Dominion.

We hope to hear much more from this study group, and in the meanwhile commend their proposals to the careful attention of every member of our profession.

H.E.M.

The Late Professor J. S. Haldane, C.H., M.D., F.R.S.

Professor Haldane died at midnight, March 14-15, 1936. It is impossible in a short compass to do justice to his character and attainments. He was a super-man and a member of a super-family. The late Professor Sir John Burdon Sanderson was his uncle; Viscount Haldane of Cloan and Sir W. S. Haldane, W.S., were brothers; Miss Elizabeth Haldane, C.H., was a sister; J. B. S. Haldane, F.R.S., professor of genetics in the University of London, is his son; and Mrs. Naomi Mitchison, a well-known novelist, is his daughter.

John Scott Haldane was born in Edinburgh on May 2, 1860, the son of Robert Haldane of Cloan, Auchterarder, Perthshire, and Mary, daughter of Richard Burdon Sanderson. He was educated at Edinburgh Academy, Edinburgh University, and the University of Jena. He took his medical degree at Edinburgh in 1884. Early he became interested in the physiology of respiration and remained interested in various physiological problems for the rest of his life. He became demonstrator of physiological chemistry at Oxford in 1887, under his

uncle, and remained at that University until his death.

Haldane's very important work at Oxford dealt with problems of pure physiology and industrial hygiene. He investigated the impurities in the air of mines and their effects on the health of man. He devised a most valuable test for the presence of small amounts of carbon monoxide. He studied the anæmia of Cornish miners, miner's phthisis, and ankylostomiasis. Ventilation as a hygienic problem also engaged his attention. In 1905 he began an investigation for the Admiralty of the subject of diving, and, notably studied "caisson disease". In the latter connection he devised a method of "stage decompression" which obviated the risks from submersion under high pressure.

During the Great War Haldane was a member of a Committee appointed to enquire into the physiological needs of the soldier in the matter of food, clothing and training, this work being followed by a radical change in the scale of rations for active service. He also introduced methods of dealing with poison gas, and devised an efficient portable apparatus for the administration of oxygen, which proved to be useful also in ordinary medical practice.

In a fundamental work on respiration, published in the *Journal of Physiology* in 1905, Haldane gave for the first time a rational explanation of the automatic changes in respiration associated with changes in muscular activity, and laid the foundation for methods of resuscitation after failure of respiration which are of great clinical value.

From the philosophic side, it may be remarked that Haldane saw clearly that "physiological phenomena are meaningless when investigated singly and can only be understood when the organism is studied as a whole". As he put it, the phenomena of life "express the maintenance of a coordinated whole, which includes within itself relations to environment as well as the mutual relationships of details of internal structure and activity".

Professor Haldane was elected a Fellow of the Royal Society in 1897, a Fellow of New College in 1901, and a Reader in Physiology at Oxford in 1907. He was awarded a Royal Medal in 1916 for his work on respiration, and in 1934 the Copley Medal of the Royal Society for his application of physiology to the practical problems associated with medicine, diving, mining and engineering. He also received Gold Medals from the Institution of Mining Engineers, the Royal Society of Medicine, the Royal College of Physicians, and the North of England Institute of Mining Engineers. He had also many honorary degrees, including some from Edinburgh, Birmingham, Oxford, Cambridge, Leeds, Dublin and Witwatersrand. A.G.N.

Sir Charles Alfred Ballance, K.C.M.G., C.B., M.S., F.R.C.S.

Sir Charles Ballance, of London, the well-known otologist and neurological surgeon died on February 8th last.

Ballance was born in 1856, educated privately and at St. Thomas's Hospital, taking his degrees in the London University (Gold Medals in both the B.S. and M.S. examinations). He then proceeded to the F.R.C.S.(Eng.). After a period of post-graduate study he was appointed to the staff of St. Thomas's, and in addition to his general surgical work took charge of the Ear Department. A man of vision and of an original cast of mind Ballance soon made his presence felt. He was one of the first, if not the first, in England to perform the complete mastoid operation, including ligation of the jugular vein and drainage of the lateral sinus. In this connection, also, he suggested the practice of grafting, which has been found of so much value. Later Ballance was appointed to the National Hospital for the Paralyzed and Epileptic, Queen Square, where he was colleague with Sir Victor Horsley. Always keen in research, he introduced some valuable procedures, based on experimental study. Such were the ligation of arteries and its bearing on the treatment of aneurysm, and the grafting of nerves, particularly in connection with the subject of facial paralysis. He also made a study of the anatomical relationships of the temporal bone.

In 1912 Ballance became chief surgeon to the Metropolitan Police, a position which he held until 1926. During the Great War he served as consulting surgeon with the rank of Colonel. He received the K.C.M.G. and became a Knight of Grace of the Order of St. John of Jerusalem. He held honorary degrees from the Universities of Glasgow and Malta. He delivered the Bradshaw and Vicary Lectures, and, in 1933, the Lister Memorial Lecture. He was the first president of the Society of British Neurological Surgeons.

Sir Charles Ballance was held in high esteem, both for his personal qualities and scientific attainment, in Canada, where he was well known, as in England. A.G.N.

British Health Resorts—Spa, Seaside, Inland*

This publication is an annual visitor. It is the official handbook of the British Health Resorts Association, of which body Dr. Alfred Cox is the General Secretary. The book, which is put out at an absurdly small price, is edited for the Association by Dr. R. Fortescue Fox,

* British Health Resorts. 290 pp. Price, 1s. net. London, J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Square, 1936.

and is compiled from information supplied by Medical Officers of Health, Local Authorities, and individual contributors. The material has been revised by a Medical Advisory Committee, representing various bodies; in the list of members we note such names as Lt.-Col. W. Byam (Chairman), Lord Horder, Sir Humphry Rolleston, Sir Holburt Waring, Sir William Willcox, Mr. L. R. Braithwaite, Dr. E. K. Le Fleming, and Dr. Rupert Waterhouse. The information provided can, therefore, be regarded as authoritative. To quote from the preface by the Minister of Health, the Rt. Hon. Sir H. Kingsley Wood, "The task which the Association has undertaken is threefold: to bring before the public the claims of British spas and watering places to possess curative resources in no way inferior to continental health resorts; to offer to the medical profession and its clients expert advice on the natural conditions most favourable to the successful treatment of the maladies with which they are concerned; and to inform them where these conditions may be found in this country."

The publication includes not only the health resorts of Great Britain and Ireland but those of Australia, the British West Indies, Canada, New Zealand and South Africa. The resorts are classified alphabetically, and detailed in-

formation is given as to geography, climatology, and the suitability of the particular place for the treatment of various diseases. There is a useful introductory discussion of the different ailments for which spa treatment is advisable. This section is most helpful. A note on hotels has been added. One could wish that Canada could make a better showing. There are numerous places here to which invalids may go, with a variety of climates, but there are few where there is a systematic attempt to utilize to the full the undeniable virtues of the particular location. The best known of these are the Banff Hot Springs in Alberta, the Harrison Hot Sulphur Springs in British Columbia, and the several sanatoria at St. Catharines, Ont. The possibilities of the situation are considerable, but, at the moment, Canada is chiefly looked upon as a great and delightful playground for the well.

After reading the work here described one can have little doubt that the British Empire can provide excellent facilities for dealing with those diseases that are amenable to climatic and spa treatment, and that there is no need for medical men to advise their patients to go to foreign countries. Get this book. It is well worth study.

A.G.N.

Special Article

THE CONTROL OF NARCOTICS

By C. P. BROWN, M.A., M.B., D.P.H. AND
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It has been suggested that information as to the control, both international and domestic, of the various narcotics which are included in the armamentarium of the practising physician would be of general interest to the medical profession, and in this paper an endeavour is made to indicate the methods employed both in relation to the administration of the various International Narcotic Conventions and to the practical application thereof in Canada.

In so far as opium is concerned, Turkey and Yugoslavia produce most of that used for legitimate drug manufacture, Greece and Bulgaria also produce some, while Japan and Russia grow some for their own use. Persia, China and India grow most of that used for smoking and for eating. India, however, has reduced her export 10 per cent annually since 1926, and that export ceased entirely at the end of 1935. Probably 90 per cent of the world's opium production is

grown in China. Most of the coca leaf is grown in Java, Peru and Bolivia, with some production in Japan and Formosa. Indian hemp (*Cannabis*) is grown in most parts of the world. The chief drug manufacturing countries are France, Germany, Holland, Switzerland, Great Britain, Japan and the United States. The last named country manufactures almost exclusively for internal consumption. Canada does not manufacture any of the basic drugs, but imports from abroad, as necessary.

Under the terms of the International Conventions, each country furnishes annually to Geneva estimates of its legitimate requirements in respect of each drug, together with full explanations as to the manner in which these are arrived at. In Canada, for example, the basis is that of consumption during the previous year, which is estimated from stocks in the hands of our 106 wholesalers at the end of each year. These inventories are known to be reliable, as a Government narcotic auditor devotes his whole time to auditing the stocks and transactions of the licensed wholesalers. The estimates of all countries are examined and passed upon at Geneva by a Supervisory Body consisting of four persons, nominated by different countries, and so constituted as to include both medical and administrative experience. This Body has no

power to revise an estimate without the consent of the Government concerned, but is empowered to ask for explanations, and has already in a number of cases succeeded in inducing Governments to reduce estimates which were obviously excessive.

Although fifty-three countries are parties to the Narcotic Limitation Convention, there are still a few who are not, but they also are invited to furnish estimates. If they do not, the Supervisory Body does it for them, and while of course such estimates cannot be made binding upon non-members, the countries subscribing to the Convention are so bound in relation to exports to such countries. A country therefore which is not a party to the Convention can only obtain drugs in excess of the estimates prepared for them from a country which is also not a party. In practice this produces excellent results, for all exporting countries are members. During 1933 world manufacture of narcotics was less than world consumption.

At the conclusion of the examination of all estimates the Supervisory Body issues for the guidance of all Governments a statement containing the estimates as settled for each country, and all world transactions are required to be within the limits of such estimates. The movements of narcotics between countries are under the very strict import and export license system which provides that exports shall not leave any country until the Government of the importing country has delivered an import license indicating its consent to certain definite importations. If the transaction is within the limit of the estimates, an export certificate is issued, which accompanies the shipment. The latter upon arrival is checked by the customs authorities of the importing country, and the export certificate is eventually returned to the Government which issued it, with an endorsement thereon indicating the narcotics actually received. In addition, special procedure is followed in regard to heroin, in that countries desiring to import this drug must make a special additional request therefor to the Government of the exporting country, and can only issue an import license in favour of a Government department, instead of to a firm of licensed wholesalers. In this way the importing Government assumes special responsibility in regard to heroin, and undertakes to strictly supervise its subsequent distribution.

All imports and exports of narcotics are reported quarterly to Geneva, which enables a close check to be kept there on international traffic. All countries are notified when the estimates of any country have been exceeded, in which case exports to that country immediately cease. This control is far from being a formal one; Canada, for example, has on several occasions been called upon to explain apparent discrepancies between her reported imports and the quantities reported by other countries as having

been exported to her, the explanation usually being that the drugs were despatched from Europe in one quarter and arrived in Canada in the next.

Each country is also obligated to maintain a special organization to control narcotics from both the legal and illicit angles. In giving effect to the former, a somewhat elaborate machinery is necessary in Canada. All narcotic sales by each of the 106 licensed wholesalers are reported monthly to the Narcotic Division of the Department of Pensions and National Health, such sales of morphine, heroin or cocaine, except to other licensed wholesalers, being limited to one ounce of each drug per month to each individual drug store, physician, dentist or veterinary surgeon, a maximum which is in most instances not approached, but which may be occasionally exceeded on special authority being issued. The same maximum is applied to codeine in so far as sales to retail druggists are concerned.

Upon receipt of sales reports at Ottawa, each transaction is transferred to the individual cards maintained for each physician, dentist, veterinary surgeon and retail druggist in Canada. No entry can be made on a card unless there is a previous indication thereon that the person concerned is "licensed and in good standing" as required by the Narcotic Act. This information is obtained by the much appreciated cooperation of the thirty-seven Registrars of the organizations concerned in the nine Provinces, who regularly supply lists of additions, subtractions, changes of address, etc., re their members. Any sale to one not eligible is immediately taken up both with the wholesaler and the individual concerned, and a stop order issued until the situation is regularized. The necessity for strict checking in this regard was made manifest at the outset by the number of cases discovered in which persons without any qualifications at all had been deceiving wholesalers by false claims to eligibility. The rigidity of the application of the law in this respect, while completely necessary if control is to be maintained, has its compensations for the Provincial Medical Associations, as many physicians previously inclined to be lax in keeping themselves in "good standing" now either pay their fees promptly, or repair their omission upon receipt of a tactful letter from the Narcotic Division advising them of their temporary ineligibility to purchase narcotics.

In addition to the records of wholesale purchases already referred to, there is a periodic check of all retail drug stores. Their sales reports are also tabulated. The final cards covering all purchases made by physicians, veterinary surgeons and dentists are regularly studied, and where totals appear to be high enquiries are made by correspondence with the practitioner concerned. As a result we have many hundreds of cases in which we know of the need for the

narcotics obtained in the purely legitimate practice of medicine, which obviously precludes any necessity for future enquiries, but it is nevertheless a fact that this close checking does disclose a considerable number of cases in which the narcotics involved are either being used illegally or unnecessarily. Cases of that kind and those in relation to which there is the slightest doubt are carefully examined by a medical officer of the Department, and it is felt that a recital of some of the conditions encountered would not only be of interest to the profession but a good indication of the necessity for this angle of narcotic control, the ultimate result of which, where conditions warrant such action, is the inclusion of the name of the professional man concerned in the Confidential Restricted List, which renders it impossible for him to obtain narcotics from wholesale or retail sources. These case files containing the information furnished by the practitioners, on consideration by the medical officer, eventually resolve themselves into the following groups.

First, where the physician gives a perfectly satisfactory explanation as having under his care one or more patients legitimately requiring large amounts of narcotics, usually involving terminal conditions not susceptible of relief in other ways. These are cases in which the Department has neither the right nor the desire to interfere, and the matter is closed with an expression of thanks to the physician for his co-operation.

The second group is composed of those who use an excessive amount of narcotics in general practice, without any suspicion of bad faith, but in our opinion with poor judgment. In one instance a physician had used 1,600 grains of heroin during the year under review. He resented our enquiry, replying that his use of heroin had been both ethical and legal in every way, that he had used it only on selected cases and to procure a definite result, and that he had taken full precautions against addiction. He had a small town and rural practice. Another physician in a small city, specializing in nose and throat, and venereal disease, was using 200 grains of cocaine monthly. He explained this by his general use of electro-therapy, and especially the electro-coagulation of tonsils. He also claimed to use it in solutions up to 15 per cent strength for injection into the urethra in acute gonorrhœa.

The third group uses narcotics improperly in treating conditions such as asthma, rheumatism, migraine, chronic alcoholism, etc., thereby invariably producing or accentuating addiction. One physician treated a patient for four years, suffering from an indefinite complaint of the liver and bowels, supplying him with a syringe and morphia for self-administration, until he was finally taking $9\frac{1}{2}$ grains per day. Similarly, another physician had prescribed morphia for a

patient from asthma for many years, eventually reaching 9 grains per day. To our repeated remonstrances he refused to pay heed further than to reduce the dosage to 7 and $2/5$ th grains per day. The Department then intervened, making it impossible for this doctor to prescribe further. As a result, the patient was admitted to hospital with a diagnosis of asthma and morphinomania, and after a month's treatment was greatly improved and on a dosage of two grains daily.

The fourth is a group representing the improper and frequently illegal treatment of addicts by the ambulatory method. The patient may first appeal to the physician as suffering severely from withdrawal symptoms, or pleads some chronic or even acute illness as justifying his request for narcotics. This Department has abundant evidence on record to show that these cases have very seldom any intention of ceasing their addiction. They submit themselves to the reduction treatment only until such reduction is sufficient to cause serious inconvenience, when they leave the supplying physician and attempt to find another from whom they can take another treatment commencing with a higher dosage. They also shop around amongst other physicians during the treatment, and thus achieve a higher total dosage than that initially obtained, the balance frequently being sold to other addicts. Once an addict succeeds in locating such a physician, the news spreads through the underworld and others flock to his office. Such physicians are merely replacing the trafficker. It is sometimes difficult to believe in their good faith, in view of the long period of treatment, the obvious slight reduction, if any, effected, and the absence of cures. One physician prescribed 8 grains of morphia daily for 79 days to a single patient, without any medical condition. Another reported nine cases under treatment for a considerable time without cure. Another, after four years' correspondence, reported eight patients then under treatment, of whom three appear on the files of the Department as well known morphine addicts. After two years' correspondence, another physician reported eleven morphine addicts then under treatment, of whom Departmental files showed four had police records. Another reported twelve known addicts under treatment, of whom Departmental records showed five were criminals. No cures were reported. This but confirms the opinion held in practically all countries that treatment by the so-called ambulatory method is generally doomed to failure.

A fifth group is composed of those whose explanations are obviously false. One physician, on enquiry, stated that he had prescribed 70 grains of cocaine for a confinement case, injecting 12 grains one day and 22 grains the following day into the cervix to produce dilatation, with, he stated, a happy outcome; and using a

further 12 grains for a local repair two weeks later, the remaining 24 grains not being used. A dentist attempted to justify the use of 200 grains of morphine per month by explaining that he was specializing in dental surgery. His methods as outlined were strongly condemned by one of our leading university dental faculties with whom we communicated. In reality he was purchasing more than double the amount stated.

A sixth group supplies narcotics entirely improperly and illegally in large quantities to transients. A physician in a small country town so supplied 106 grains of morphia in nine days, for self-administration, to transients whom he reported as stating they were suffering from such conditions as migraine and pleurisy. A seventh group might include those physicians who plead theft of their supplies, after displaying gross carelessness in guarding them, such as by leaving them all night in an automobile, with the window open, on the public highway.

No discussion of the use of narcotics should omit special mention of heroin. The consensus is that its use can be justified only in obstetrical work and in certain selected types of obstinate cough, such as that accompanying terminal tuberculosis, and, then, in proper dosage. It is universally conceded to be the most dangerous of all the habit-forming drugs. Its use is prohibited in a number of countries, and it is subjected to special control measures in relation to its international movement. Its general use for narcotic purposes, almost to the exclusion of other drugs, cannot be justified.

The danger of codeine to anyone with an addiction temperament, or who has previously been addicted to other drugs, is most emphatically stressed. There is abundant evidence that codeine is being extensively used in Canada in dosages so far exceeding legitimate medical needs as to warrant the assumption that addiction does result. This confirms the opinion expressed by Dr. David Slight in his article on "Codeine addiction", appearing in this *Journal* (1935, 32: 69).

This analysis would be incomplete without reference to the, fortunately, small number of practitioners who sell narcotics to the underworld, often at the regular trafficker's price of one dollar per grain. The popularity of this source of supply in underworld circles is accentuated by the fact that narcotics so obtained are usually free from adulteration. Instances of this type certainly merit and receive police action. It is only in aggravated cases where *mala fides* is obvious that Court action is taken, and it is emphasized that the Narcotic Division does not permit the employment of addicts to trap physicians, nor does it authorize the investigation of a physician unless definite suspicion exists in the particular case. The former ruling certainly adds to the difficulties encountered, but is more than compensated for by the knowledge

that the Department is "playing fair" with the medical profession, and that if a physician, already under suspicion, chooses to sell narcotics to a definitely healthy person and gets into trouble as a result, he cannot blame the authorities for putting a stop to his activities. It is the policy of the Department not to take drastic action if effective results can be achieved by any other possible means. It is perhaps appropriate to quote the words of Dr. Amyot, the late Deputy Minister of Health, which, although uttered in 1927, hold good today, "Practise legitimate medicine and you need not even think of the law."

It will be noted that this article is prepared in conjunction by a physician and a layman, as both have their very definite spheres in relation to the subject. Both, however, insist that no article in relation to narcotic control for publication in a medical journal in Canada would be complete, or indeed give a correct picture, if reference were not made to the very great assistance received from many members of the medical profession. Frequently, and in most instances without any possible hope of material reward, they contribute much time and infinite patience in an endeavour to help those who are in the toils of narcotic addiction, and who, by means of their position in the community, have some chance of rehabilitation, and the Narcotic Division welcomes the opportunity to pay tribute to their work.

THE MEDICAL MAN'S STANDPOINT*

By A. H. GORDON, M.D.,

Montreal

"The Medical Man's Standpoint" is like the Speech from the throne: a member may talk on any subject or on no subject in its discussion, and not be out of order.

I was brought up with four brothers in a minister's family, where the total income was less than it costs me now to run my office, and still my parents never went into debt, and if I didn't learn medical economics I learned ministerial economics, and know full well what "unpredictable expenses" meant to that household.

Before coming to college, I worked for five years, commencing at a dollar a week and winding up in a blaze of twenty-five dollars a month, and so learned what money costs in work to the working man, or boy; and this reminds me of an address by a late manager of the Bank of Montreal, in which he said "When I recall what 25 cents meant to me as a boy, I am amazed at the cheerful abandon with which the youth of the present day will spend five dollars."

* This paper formed part of a symposium on "The problems of social medicine", at the Montreal Medico-Chirurgical Society, on April 19, 1936.

After graduation I worked for two years at \$100 a month as assistant to a doctor in British Columbia who had charge of the medical work of a coal mine, and there learned some of the advantages and a great many of the disadvantages of contract work in medicine.

I did general practice for so long that I can't get away from the obsession that a patient is a human being. In my first three years in Montreal I didn't make my office expenses, and my first year's gross income was \$180.00.

Incidentally, in the last 35 years, I have held jobs from intern up in a large public hospital, until through lapse of time and the retirement of my seniors, I find myself teaching students and attending such patients as the hospital entrusts to my care.

During these years it has been the accepted practice of the staff to attend everyone whom the hospital admits, to work late and early, to do one's best and confine one's grouching to a little mild martyrdom at the lunch table, but one was always ready to be promoted to the opportunity of doing more work, and the idea of losing a hospital job was akin to a sentence of death.

The only excuse for reciting all this personal history is that it has coloured any views I have upon the relation between doctor and patient, and upon the subject of medical economics in general.

Few of us realize that during these later years, the faint hum which was heard from time to time in medical circles borne upon the west wind, was really the sound of a going in the tops of the mulberry trees and that it was the commencement of a strong wind of discontent with things as they are.

Presumably the court at Versailles heard clinking sounds in the distance, and not till later did they know that they were the sounds of the knitting needles in the hands of many Mesdames Lafarge, and that the old order was changing to give place to new. I would like to quote a paragraph from a minority statement in the report on "Medical Care for the American People":—

"The concern of this investigation is the performance of a great social function,—that of keeping the people in health; this is the beginning and the end of the problem of medical organization, all else that is considered here—physicians, nurses, hospitals, clinics, the drug trade and the like—are agencies whose value comes from the efficiency and adequacy with which they contribute to that end. There is nothing final in any of these agencies, none of them in its current form is to be taken for granted in the discussion. The professional services which medicine has to offer may be made available to the public under any one of a number of distinctive sets of arrangements. A sharp distinction between the technology of medicine and its organization is essential to adequate analysis. The organization of medicine is not a thing apart, which can be subjected to study in isolation—The ways and means for putting medicine in order must take account of the conditions of life and work among the people whom we serve."

This summary is a useful statement of the present case of medical economics. Let us take

first the concept of "A great social function—that of keeping the people in health." What criticism may the mass of the people make upon the performance of that function in Montreal at the present time?

(1) If I am apparently well no one worries about me, but all the time I may have cancer, tuberculosis, old age, nephritis or flat feet, and it is only by accident that they are discovered, and for some of these things something might be done. (2) If I am ill I can't afford medical treatment, and if I'm ill for a long time, the expense will set me back for years. (3) There are many doctors who haven't enough patients to give them a living, and all about them are many patients who can't afford to have a doctor.

These justifiable criticisms and many others which one could cite, indicate that while the technology of medicine is relatively sound its organization is cumbersome and inequitable and does not measure up to the definition of "a great social function—that of keeping the people in health".

In regard to the technology of medicine—even a die-hard like myself in emphasis upon the strictly clinical in medicine cannot help but hear the hum of the machine in the distance. I feel sure that the time is not far away when medicine will be more and more mechanized and materialized, and when mass production by newer methods in physics and chemistry will eliminate many of our laborious individual methods of diagnosis and treatment.

The x-ray and the electrocardiograph and the sound recorder and the chemical laboratory even now can almost make a diagnosis, and when a history can be taken by a psychological lie detector, even the squeal of the biped can be salvaged and made use of, and our present person to person method will be as much superseded as the paint brush has been by the power spray in painting a flock of motor cars. Many of you may see these things and participate in them, and perhaps even press a button in the new machine.

One can imagine a cavalryman of the last generation bemoaning the coming of mechanized armies because they would take the glory out of war, but he must remember that there was a time when cavalry doubled the speed of infantry. "For men have two feet and horses have four feet, and two into four goes twice", but the motor in war has no speed limit. The old order changeth, yielding place to new—lest one good custom should corrupt the world.

One cannot conceive, however, that a time shall ever come, even after the inefficiencies and the circumlocutions of our present methods have been abolished, when there will not be a place in the new mechanized and physcized era for trained observation and logical deduction, which have been the crown and flower of what we may call the Oslerian age.

No matter how accurate and how efficient the machine may be, it will some time slip a cog and trained commonsense must come to the rescue. You will know the story, told in many forms, of the northern motorists in the south, who were on the wrong road and asked a small country lad the way to one town—he didn't know, then they asked him the way to another, and he didn't know that. The driver said "You don't seem to know much." "No," said the boy, "I don't know much, but I ain't lost."

Many of us live in a chronic fear of change: new things look like the bogey man. Any sort of alteration in the *status quo*, gives us the mental pip. But changes will come and even our crystallized form of attempting to heal the sick is in for a change.

Our present method of rugged individualism is going to be shaken, but some of its desirable things will remain. Why should Dr. X, who lives in Westmount, spend part of his day travelling to St. Lambert to see one patient, and then to Maisonneuve to see another, while Dr. Y of St. Lambert goes to Westmount to see a patient who has moved over from the mainland?

Why should the man who has chosen the honourable career of a general practitioner be rewarded with two dollars for recognizing an attack of acute appendicitis, while his classmate who operates upon him collects two hundred? True the general practitioner is invited to come to the operation and wear a cap and gown and do so without either fear or hope of reward.

If the bookkeeper who is operated upon and who doesn't dare to go into a public ward on account of his wife's friends, gets a pelvic abscess or a phlebitis after his operation, and remains in a private room in a hospital for six weeks, at six dollars a day plus surgical fees and extras, who is going to measure the economic tragedy which has overtaken him?

Or what shall it profit the farmer in the country when his doctor calls a consultant from the city to confirm a diagnosis of inoperable carcinoma or a fatal pneumonia, and what shall it profit the city doctor when he must hang his head as he mentions the fee he must charge for his day's or night's journey. All these things are reasons for a change from our present system to some form of cooperative medicine, Government controlled or otherwise.

I know the dangers of removing individual initiative. In two years working in a contract practice, I realized what a benumbing effect such work may have upon the medical mind and how difficult it is not to fall into routine and slipshod ways.

I know what havoc a government controlled railway has brought to this country, and I too have waited at the customs parcel window in the post office for the leisurely and cynical government official to stroll towards me and accept my card with the air of an emperor disturbed at

his luncheon. But in spite of these sad facts we must see to it that the waste of time, the waste of money, the waste of effort and the waste of health in our present system are checked, and a better distribution of medical benefit is planned for the people at large.

From these remarks you will gather that I believe that all is not well with medicine on the economic front. From the standpoint of a medical man with the background which I have detailed to you, I am sorry for the doctor, but sorer still for the patient.

The unpredictable calamity is not one which the individual should be called upon to bear alone. Insurance against fire, against hail, against shipwreck, and against death, have all helped to make life more bearable, and why not insurance against illness for all people below a certain level of income, or, for that matter, for everyone? Even as insurance against public liability should be compulsory to all motorists.

It would appear essential that in such a plan there should be complete freedom for the insured to choose any qualified practitioner, he to be paid from the public treasury on the basis of work done.

This would involve the return of the general practitioner to his own, and he would be required to be in training and fitness the equal of any man in the profession; and since he would be the king-pin in the new machine, his qualifications should be subject to visa from time to time, for his would be the responsibility of providing for his clientèle the most approved and most modern methods of our art.

Inevitably the premiums for this insurance will be levied upon the taxpayers, according to their ability to pay, for the poor cannot pay what it will cost to give them a sufficient medical service, and the whole country must pay for the medical care of the indigent. All this will, of course, tickle the taxpayers, of whom you and I will be a part.

The fear of change, which I mentioned a while ago, is often mixed up with fear of people called radicals and that is mostly groundless. Briand, the fire-eating Socialist of the extreme left, saved France from internal explosion and saved Europe from new wars. Ramsay MacDonald, looked on as a wild-eyed radical when out of power became the leader of a Tory Government in power. We would be saddened, but not surprised, to see Mr. Woodsworth when he becomes Prime Minister of Canada, turn up in Parliament on a Monday morning with a chin as bare as Mr. King's or Mr. Bennett's. The wearing of whiskers and the eating of fire are usually self-limited disorders.

Having said all this I am mindful of the words of a writer in a recent number of the *Atlantic Monthly*—"Making speeches about unemployment insurance, old age insurance and the general desirability of social security involves no

great difficulty, but drawing the specifications for a law which shall be other than a mad-house mess on either of these topics, is a different matter." I am quite certain that health insurance offers no exception to this statement.

The final sentence of the paragraph which I quoted some time ago, reads as follows: "The ways and means for putting medicine in order must take account of the conditions of life and work among the people whom we serve." This implies that plans proposed for a new district or for a widely scattered community or for a small town will differ from those applicable to an old established district or a large centre where the care of the sick has been organized for years around large hospitals and universities.

Perhaps a few words of personal impression in regard to the City of Montreal may not be out of place: The first hospital to be opened in Montreal, the Hôtel Dieu, "The House of God", and each succeeding hospital, with few exceptions, has been opened as a charitable institution made possible by the free gifts of citizens and manned by the free labours of physicians. Such hospitals are the background of the medical "conditions of life and work among the people whom we serve," and there hasn't yet come a time when these hospitals could not be manned

by the free labours of physicians. The time may come when it is no longer possible, but I hope I shall by that time have passed into an innocuous desuetude, and while I feel strongly that the care of the indigents outside the hospitals should be a charge upon the public, it appears to me contrary to the spirit of our hospitals since their inception that the medical attendants should receive remuneration for the care of public patients in hospital, any more than that the heirs of the original contributors to the institutions should receive dividends upon the sums donated by their ancestors.

There are now on foot in all hospitals, methods which aim at preventing the abuse of hospital charity, and these methods may quite possibly be improved, but it is a reasonable assumption that anyone who will stand in line at a dispensary wicket and then take his turn for admission to a clinic has a good financial reason for doing so.

For the medical attendants in a public hospital there is a *quid pro quo* in widened experience, in association with like-minded members of the staff and a sense of duty done, which in themselves are a substantial reward, and which keep a man for the hours of the day thus employed in the atmosphere of the priesthood of medicine.

Medical Economics

Proposed Plans for the Security of Health in the Province of Quebec

The following paper has been prepared by the Montreal Study Group for the Security of the People's Health. This group, formed in the winter of 1935-1936, is composed of doctors, dentists, nurses, social service workers and statisticians interested in the study of the relationship of medicine and allied professions to the state in the various civilized countries of the world. These proposals are being sent out in the form of an open letter to various medical and other associations in the province and are published here for the benefit of our readers.

In view of the coming provincial elections in the Province of Quebec it would appear to be a most opportune time to put forward some definite plan or plans to the political parties seeking election, expressing the collective demands of the allied medical, dental and nursing professions. The recently instituted Unemployment Medical Relief Commission in Montreal is a step in the right direction. At the same time, other plans should be presented by the organized professions (the English and French doctors, dentists and nurses) to embrace the entire province. The following suggestions are made:—

1. It is the grave duty of the combined professions to point out to our politicians the present deplorable, yet remediable, condition of the

health of our citizens. Our knowledge of health and disease places this moral responsibility firmly on our shoulders.

2. From each political party, demands should be made that, as a prominent plank on their respective platforms, state responsibility for the health of its citizens, whether employed or otherwise, is a primary principle. A man should not lose his rights as a citizen because he loses his job.

3. That on no account an attempt be made after the election, on the false ground of economy, to abolish the present medical relief for the unemployed in Montreal.

4. That, if alterations in the present set-up of the Commission be contemplated in the future, they should tend towards increasing the amount set aside for the Commission's functioning. This is 25c. a month per person on relief. An increase to 50c. per month should be demanded.

5. That, in view of the possibility of a reduction in the monthly accounts of doctors under the Commission such reductions should be strenuously opposed unless a proportionate reduction be made in the accounts of the other recipients, *i.e.* the druggists. Here the principle that the doctor (precisely as the druggist) is selling a commodity, should be rigidly maintained. This should be the end of the exploitation of the medical profession.

6. If the proposed proportionate distribution of funds to doctors (80 per cent) and to druggists (20 per cent), dentists nil, nurses nil, on the basis of 25c. a month allocated for each unemployed, be found to be in practice out of all proportion to this, that the municipalities should set up three or more city drug dispensaries to take the exorbitant profits out of filling prescriptions, and sell drugs to its unemployed citizens at cost price. To show that such an event is not beyond possibility the experience of the Municipality of Lachine in 1935 may be quoted:—

To drug stores	\$ 9,224 =	60 per cent
To doctors	4,918 =	32 per cent
To dentists	1,263 =	8 per cent
Total	\$15,405 =	100 per cent

Under the present Montreal Commission the distribution proposed would have been as follows:

To drug stores	\$ 3,081 =	20 per cent
To doctors	12,324 =	80 per cent
To dentists	Nil =	Nil
Total	\$15,405 =	100 per cent

7. That in the event of a marked reduction of doctors' monthly accounts for service to the unemployed being made (for example, to 33 per cent or 66 per cent of their total) on the plea of the Commission's inability to pay, that the following plan be substituted. The factual basis of the following plan is founded on the figures of the Montreal Relief Commission for March:

Heads of families (men or women) unemployed	65,785
Dependents of the above	102,122
Unemployable	2,269
Total on relief	170,176

At 25c. per month, the yearly income of the Commission for medical relief for distribution to doctors and druggists is $170,176 \times 0.25 \times 12 = \$510,528.00$. Of this amount, the doctors' share will be 80 per cent—\$408,420.00. Of the 3,000 doctors in Montreal, \$08 have registered on the Commission's list. This would permit an average of \$500.00 per year for each registered doctor. If the 170,176 persons on relief would be evenly divided, each of the registered doctors would have 212 patients. The proposed plan, in the event of the probability of the breakdown of the present scheme, is as follows:—

A Central Medical Planning Board be formed by representatives of the English and French doctors, dentists and nurses. Any registered doctor in good standing in his medical society (this would be necessary for proper disciplinary control) may register with the Board and practise under this scheme. The patients should have the right of choice of doctor and also right of change at certain fixed intervals. For these doctors, accepting relief patients, abolish entirely the antiquated system of fee-for-service and substitute a per capita payment for an all-in

service. It would cost no more than the present system (25c. per month—or \$3.00 a year for each patient).

8. Not only must the present medical relief be maintained, but it must be expanded and increased to include surgical dental treatment and home-nursing. In February, 1935 (see Comparative Statement of the Relief Situation in Canadian Municipalities, 1935; Department of Social Research, McGill University) the City of Montreal had 191,778 on relief (19.5 per cent of its population). (This figure has now fallen to 170,176 in March, 1936). But on the basis of 191,778, the municipal share of the year's relief expenditure was \$5,437,000.00, which, in comparison to its annual civic revenue of \$40,927,000.00, was in the ratio of 13.3 per cent. In short, 19.5 per cent of the population on relief of Montreal has expended on them for relief 13.3 per cent of the annual revenue. In comparison, Westmount with 2.1 per cent of its population on relief distributed 2.1 per cent of its revenue; Outremont, with 1.2 per cent on relief, 2 per cent, and Lachine, with 26.8 per cent on relief, 27.6 per cent of the city's revenue. The addition of the present contemplated expenditure of \$510,528.00 for medical relief (if paid in full by the municipality itself) and if the number on relief remains comparatively stationary, would increase the total annual civic expenditure to \$5,947,528.00 and only increase the ratio of 13.3 to 13.8 per cent. If, however, an additional 25c. per month was allocated to cover dental and home nursing care this would increase the total expenditure to \$6,355,948.00 and raise the ratio of relief to civic revenue to 15.5 per cent. This figure would still be within the range of ordinary humane necessity.

Thus, an additional 25c. per month bringing medical expenditure per capita for those on relief to 50c. per month, instead of the present 25c., would cost approximately \$1,021,056.00 a year, or \$6.00 per capita on relief a year (based on the March 1936 figure of 170,000). This \$6.00, judiciously expended on a blanket health service, and not on a fee-per-service basis, would give a more nearly adequate medical, dental and nursing service and take up the slack of unemployment in the dental and nursing professions. It would encourage preventive medicine being practised, which is out of the question on the fee-per-service basis. A Central Nursing Planning Board should be set up to unify the activities of the County Health Unit Nurses, Welfare Nurses, School Nurses and Victorian Order of Nurses. There is much wasteful duplication of administration and there should be a marked extension of all the above-mentioned groups, each autonomous in its individual field but under central control.

9. The outdoor departments of our hospitals would be transformed into consultant departments. A staff fund, to be distributed equitably,

should be allocated to each hospital treating the unemployed, both in outdoor and indoor departments.

10. The present hospitalization plan under the Quebec Province Charity Act to continue, but amended to eliminate the property-owning clause.

11. That the Central Planning Board set up a medical commission to study the effect of the depression and continued unemployment with the low subsistence food allowance under relief. A physical examination of every unemployed man and woman put to work under the proposed Bonchard Plan be demanded. Continued under-nourishment, combined with inadequate clothing, will most certainly predispose many such men and women to serious illness if forced to work in unfavourable climatic conditions.

12. That, following the resolution passed by the Ontario Medical Association at their last meeting, favouring experimental programs under the auspices of the local medical societies, the following plans be tried in carefully selected localities in the Province of Quebec. These four plans are typical of the large number now under discussion all over the world, and could be used as controls to each other, in a proper scientific manner.

FIRST PLAN—MUNICIPAL MEDICINE

This would be an amplification and extension of the present full-time health unit system of the Public Health Service of the province. A full-time team of doctors, dentists, nurses, including all specialties such as surgery, gynaecology, obstetrics, paediatrics, etc., should be selected (*not* politically appointed) by a Provincial Medical Planning Board (to be set up by the medical, dental and nursing societies) and placed in a given municipality, provided with a small modern hospital (a new one to be built, or an older one modernized). They would take over and control the health, prevention and cure of disease for the entire municipal population, irrespective of economic or social grouping. All such members of this combined medico-surgical, dental, nursing group should be placed on salary. Such a team of active, keen, and highly trained men and women could be easily recruited from among the younger and more energetic members of these professions. A high sense of social responsibility would be essential for appointment. The total cost of such a plan should be borne by municipal taxes and assisted by provincial grant, if necessary. The Life Officers Association should be approached to offer their services (as they offered them in British Columbia) to work out the cost of such a scheme and place the whole on a firm actuarial basis. This is also necessary for the second plan.

SECOND PLAN—COMPULSORY HEALTH INSURANCE

Select a municipality which presents a fairly

homogeneous economic pattern of income-level groups, and where relief recipients are at an irreducible minimum. No exclusion must be made, but all wage-earners and those gainfully employed must be included, irrespective of income. Only in such a way can true mutualization of insurance be possible. The actuarial figures will determine the premiums to be paid.

THIRD PLAN—VOLUNTARY HOSPITALIZATION HEALTH INSURANCE

Voluntary hospitalization health insurance in a selected urban municipality of from 5 to 25,000 people.

FOURTH PLAN—FEE-FOR-SERVICE BASIS FOR UNEMPLOYED

Care of unemployed on a fee-for-service basis covering the entire province, based on the Essex County (Ontario) model.

13. The necessity of a province-wide plan is made evident by the speech of Honourable Norman Rogers, on The National Employment Commission (official report of House of Commons Debates) in March, 1936.

The relief situation in Quebec:—

Employable	104,220
Dependents	146,410
Unemployable ..	23,510
Farmers' families	72,350

Total 346,490 = 12 per cent of population

Percentage in relation to Dominion-wide relief
(1,233,390)

$$\frac{346,490 \times 100}{1,233,390} = 28 \text{ per cent of Canada's unemployed.}$$

The percentage of unemployable on relief in Quebec is the highest in Canada, and comprises 48.71 per cent of the total unemployable in the Dominion.

14. Reorganization of the Workmen's Compensation Commission to include a wide representation of doctors, and workers, with free choice of doctor to the injured being assured.

15. That in view of the emergency of the situation and the necessity of planning for permanent poverty, a mass meeting be called immediately by the medical societies in Montreal, of all English and French physicians, surgeons, dentists and nurses, social service workers, Public Health Officials, representatives of the Trades and Labour Council, and Federated Charities, to discuss a campaign for the election of August 17th, and formulate the demands of the professions. Only through the demands made by such a United Professional Front will the various leaders be made to realize the potential political force which the 10,000 members of the medical and allied professions in the city represent. The exploitation of the professions for years must cease. It will cease when we disclose our combined professional class strength. Action must be immediate, united and decisive!

Association Notes

The Annual Meeting

The Sixty-Seventh Annual Meeting of the Association, held at Victoria on June 22nd and succeeding days, has passed into history. While no discovery of fundamental importance was announced the papers presented were of excellent quality and of practical value. One could have wished that there had been more discussion. It seems a pity that when papers are presented which have taken much time and thought to prepare there should not be an expression of opinion, pro and con, on the part of others competent to speak to the question. The suggestion has already been in these pages that the authors of papers to be read at an annual meeting should prepare about a month or more in advance brief abstracts of their work, send these to the Central Program Committee, who would, thereupon, in the exercise of their judgment, invite a few competent persons to come to the meeting prepared to discuss the various subjects. In this way nothing is left to chance, and a free ventilation of the topics is likely to take place. We bring forward again the suggestion as worthy of consideration.

Victoria is an ideal city in which to hold a convention. The Empress Hotel, the headquarters of the Association, is adequate, most comfortable, and delightfully situated. One does not usually consider that a wharf is a suitable place for a fine hotel; but in this case the water-front is pleasing and provides a continual source of interest to the hotel clientele. Then there are the charming grounds, beautiful with trees and flowers, where one can take refuge from the madding crowd and sit in pleasant shade, perchance to muse, more likely, to doze, but always finding pleasant respite. One is tempted to recall the lotus eaters, but here there were no drones. All were busy, and busy to effect. The visitors are indeed greatly indebted to the local committees, which were indefatigable and, indeed, highly successful in their efforts to make things run smoothly.

Victoria is an "out-of-doors" city; hence, no doubt, the predominance of the garden party in the scheme of entertainment. Many of the prominent residents of the city opened their delightful homes and grounds for the delectation of the visitors and their courtesy was much appreciated.

Again, the "weather man" was gracious. While, we were informed, his work, for three weeks previously, had not been entirely satisfactory, with the advent of the visitors his brow unbent and we were favoured with perfect

weather. The attendance was gratifying, some five hundred being registered.

The General Council had many momentous matters to consider, and while the most important of them were not finally disposed of, still one noted a frank and courteous exchange of opinions which did much to clarify the issues and laid the foundations for solid advance in the near future. One thing we all realized was that the interests of medical men, no matter from whence they come, are essentially the same, and that a greater bond of unity is desirable, indeed essential, if we are to take our proper place in the body politic. One heard little or nothing of that old fetiche—provincial rights, or provincial autonomy; there was something for which we must work which transcended all that. After all, Self-preservation is the first law of Nature!

The Executive Committee met on Saturday, June 20, to deal with many important matters, in preparation for the meetings of General Council, which took place on June 22 and 23. In view of the fact that the Supplement to our *Journal*, which will describe in detail the various actions taken, will appear in the September issue, it is unnecessary at this time to do more than call attention briefly to some of the more important matters. It is hoped that the supplement will be read carefully by all our members, as only in this way is it possible for the general membership to become familiar with the activities of the Association.

The members were much gratified to learn that His Majesty King Edward had been graciously pleased to continue the patronage of the Association which he had formerly exercised as Prince of Wales. July 23rd being His Majesty's birthday, a cordial and loyal message was sent to him in recognition of the occasion.

On Monday, June 22, the General Council were the guests of the President-elect, Dr. Hermann Robertson, at a delightful luncheon at the Empress Hotel, at which Dr. J. C. Meakins, the President, delivered his valedictory address. After thanking the Association for the honour it had done him by electing him president, Professor Meakins spoke in part as follows.

"If I remember rightly it was in this City of Victoria, ten years ago, that I was first elected to a position on the Executive of the Canadian Medical Association. I must confess that up to that time I had taken little active interest in what is usually called 'organized medicine'. Therefore it was some little time before I found my feet, and I am not perfectly certain whether I have found them yet or not. One cannot help but absorb, often unconsciously, a considerable number of impressions, if not actual knowledge of the problems which confront our profession. This has been particu-

larly so with myself during the past four or five years, when I have made almost yearly argosies across the continent on behalf of post-graduate education. In fact, I seem to have been particularly active in this regard since the unfortunate withdrawal of our post-graduate benefactors, and therefore have had ample opportunity to survey conditions during these troublous years. As a result of these journeyings I have acquired certain impressions which, by the very nature of the manner of their acquisition, cannot be analyzed in the light of either scientific, or mathematical methods. But I can think of nothing better to say to you today than to express what some of these impressions have been.

"There are usually held to be three professions—the Church, the Law, and Medicine. Which is the senior service need not concern us. All are irregularly disciplined within themselves. The Law has its Bar Associations which regulate the manner of practice with a more or less heavy hand, and it is to their credit that no prisoner need be without legal advice. The Church, likewise, controls the members of its profession through Synods, Presbyteries, Conferences, etc. They also see to it that none of their flock are without religious consolation; in fact, they may be said to 'bend backwards', or, rather, push forward far afield to carry their professional services to those who may, or may not, need them. They have learned by experience in their missionary work that Medicine may unlock doors for their entrance which otherwise would be difficult to open. They have faced certain problems which at times we are apt to think are peculiarly our own. They have had their irregulars, such as Knox, Calvin, Huss, Luther, Wesley, and Campbell, and at times have dealt with them in no gentle manner. They might be compared with some of the pioneers of our own profession, such as Vesalius, Harvey, Semmelweis, Pasteur, and Lister; but most of these 'heretics of the day' have left behind them movements in religious thought or science that have greatly influenced the world. You may ask what relation these things may have to my impressions in the Canadian Medical Association. Let us review for a moment how our profession is governed or directed. In the first instance the newly-born doctor of medicine must apply for permission to practise his profession. After having given satisfactory evidence to one or other of ten bodies, and after having paid a not inconsiderable sum of money for the privilege of taking an examination of variegated and often doubtful excellence, he is permitted to go on his way. The licensing body, the so-called Colleges of Physicians and Surgeons, or the Dominion Council of Medical Licensure, have no further interest in him or his professional activities, provided he does not commit a felony. The fountains from which he may then derive professional fellowship and inspiration are the County, Provincial, or National Medical Associations. These are voluntary bodies with a voluntary membership which in few districts number a majority of the profession. They fall, therefore, into the category of organized minorities. They are without legal power, and often, in so far as unanimity of opinion or voice is concerned, remind one of what took place after the Flood: 'Go to, let us go down and there confound their languages that they may not understand one another's speech. So the Lord scattered them abroad from thence upon the face of all the earth, and they left off to build the city, and therefore is the name of it called Babel.'

"These medical societies have brought great benefits to the medical profession in spite of the handicaps under which they work; but it has been a voluntary effort. It is to them that the profession, and even the laity, turn in time of trouble, although they are without legal, local or national authority. As I mentioned a few moments ago, the legal bodies are the Colleges of Physicians and Surgeons. Into their hands has been given by the people the authority to provide the latter with an adequate and competent medical service. This is a responsibility which they cannot escape; it has been a privilege which they have jealously guarded. In fact,

an outsider might be led to conclude that we are 'the annointed of the Lord' and practise medicine by divine right. The Hippocratic Oath would still further suggest such. But with privilege comes responsibility! If the people give to the medical profession, as represented by the Colleges of Physicians and Surgeons, the monopoly for the care of the sick it is only right and proper that they should expect an adequate service from those who hold such a monopoly. In this regard many of the duties which should rightfully rest on the shoulders of the Colleges have been voluntarily assumed by the medical associations or societies.

"The practice of medicine has changed considerably in the past generation and will continue to do so at a more rapid pace in the future. Parallel with this there has been also a great evolution—nay, revolution—in our society as a whole. One does not need to go into detail; it is quite obvious to anyone who looks about him or looks farther afield. The principal phase which need concern us at the moment is the relation of the medical profession to the public. They have given to us as they have given to the lawyers, and to a less extent to the Church, a fiat to provide them with an efficient and all-inclusive medical service. If the organized or regular profession fails to carry out this responsibility it is quite within the rights of the people to cancel this contract and to turn to other agencies. The public has no concern with the medical societies; they did not create them; they cannot control them. They are independent bodies, and with their independence goes their lack of legal responsibility although they may feel as individuals a moral one towards their clientèle. If the people do not get medical service it is perfectly within their rights to employ physicians, either individually or collectively, at any bargain price which they can get. Any criticism levelled at them can be quite justifiably answered by the statement that the medical profession has not given them the services that they should expect.

"These are some of the things which have been forcibly impressed upon me during recent years. The solution, to my mind, is in our own hands. We must put our house in order. We must speak one language. Our actions must be fair to all, and as a guild who have demanded and have been given certain privileges we must accept the responsibilities, and fulfil the latter if we demand the former.

"I have seen many instances where barefaced attempts have been made to exploit the doctor; to take it for granted that he is a perpetual source of compulsory charity. There has been indignant surprise that he should mildly protest, and he has been accused of supporting or being part of the closest trades-union in the world—an obviously stupid contention when the facts are known.

"On the other hand, when a certain community agreed to pay a pittance, but all they thought they could afford, towards medical care for the unemployed, certain of our profession opened new offices in industrial districts and sent agents to solicit prospective patients. I leave you to conclude what an impression such actions would create in the minds of many. If the medical profession tolerate hucksters within their midst we must expect to lose the dignity of a profession which can be trusted to discipline its members. Unfortunately, such actions cast a cloud of suspicion over thousands of others who through times of poverty and misfortune have been faithful to their trust and have stood by their people without thought of immediate, and little hope of future, monetary reward. Upright ethics are not in books or in codes but in men's hearts.

"The world is faced by certain problems, both sociological and economic, which seem to be creating chaos. There will probably be temporary improvement but there is little sign on the social horizon that they will be permanently solved by present methods. We need not concern ourselves with all of them, but only with a few that are closely related after a manner, namely, mechanization of industry, reduced requirement

of man-power, increasing population, and longevity. These are not medical problems but we are to a great extent responsible for the last two. We have steadily reduced the morbidity and mortality of infantile and infectious diseases, including tuberculosis, and are making strenuous efforts to control the rising death rate from cancer and cardiovascular diseases. But note, our battle-front has shifted from the first decade of life to the last four. There is probably no less illness in the world, but it occurs at different age-periods. The child knew little of life and was inarticulate in its protests against death. The person above forty not only demands life but he demands a living. He does not thank us to save him from tuberculosis and force him to starve because the rising hordes of the younger generation demand his job.

"We have heard much of late concerning medical economics. There is no such thing! It is merely part of the economic chaos of the times which we have helped to bring about. You may say its solution rests with politicians. Never!! A statesman, Yes! But never a politician, who is inherently an individualist, while the other is a humanitarian.

"Let us bend our minds as a profession and as an educated section of our nation to a solution of the problems which we have helped to create. We are apt to be blinded by detail and to lose sight of the great principles which make for the welfare of our people. If we have no statesmen to lead, we must at least try to adopt a statesman-like outlook. I do not suggest we should reform the world. Henry David Thoreau set down a conviction, induced by a long sojourn in a centre of enlightenment, that 'if anything ail a man so that he does not perform his functions, if he have a pain in his bowels even—for that is the seat of sympathy—he forthwith sets about reforming—the World! But I would propose, rather, to paraphrase the words of Abraham Lincoln, when he hoped to weld together a nation torn by a bitter division of ideals. He spoke to this nation, of which he knew he was but a paltry part, that their salvation rested in a mutual benignity and understanding, and exhorted them to continue their life

With malice toward none
And charity to all.

And here I divert—That the private practice of medicine shall not perish from the earth but shall continue with a wise comprehension of the duties and responsibilities of the medical profession to themselves and their people.

"To such ideals I believe we should give loyal and unflinching support."

On Wednesday evening the formal installation of the new president took place before a capacity audience, composed of members, their friends, and those occupying official positions in the community. For the first time the new rules as to ceremonial and procedure were put into effect, and all will agree that the occasion gained in dignity and picturesqueness as a consequence. After an invocation by His Lordship, the Bishop of Columbia, the visitors were welcomed by His Honour, the Lieut.-Governor of British Columbia. Dr. Hermann Robertson, of Victoria, was then installed as president by Dr. J. C. Meakins with a few well-chosen remarks, and Dr. Robertson briefly replied. Dr. Ralph A. Fenton, of Portland, Ore., brought the greetings of the American Medical Association. Much regret was expressed on hearing the news of the death, on June 20th, of Dr. James Tate Mason, of Seattle, Wash., the president of our sister Association.

A feature of special interest was the presentation of the Frederic Newton Gisborne Starr Gold Medal, for preeminent services to the cause of medicine in Canada, to Sir Frederick Banting, Dr. J. B. Collip, and Dr. C. H. Best. Fortunately, Mrs. Starr was able to be present and, after a few feeling and appropriate remarks, made the presentation in person. The late Dr. Starr had devoted many years of his life to the work of our Association and had attained its highest offices so that it is very fitting that his memory should be honoured in this way. Our grateful thanks are due Mrs. Starr for making such a thing possible.

After the meeting Dr. and Mrs. Robertson held a reception which was largely attended, after which dancing and bridge were indulged in.

During the five days of the meeting entertainments, both public and private, were abundant and delightful. The thanks of the Association are offered to His Honour the Lieut.-Governor of British Columbia and Mrs. Hamber, to the President, Dr. Hermann Robertson, and Mrs. Robertson, to Lady Barnard, to Mrs. Norman Yarrow and Mrs. J. W. Spencer, to Mr. and Mrs. R. P. Butchart, to Mrs. James Dunsmuir, for receptions and garden parties. Dr. and Mrs. E. W. Boak also very kindly entertained the members of the Executive at their country house on the Sunday preceding the opening of the meeting.

Dr. W. E. Harper, of the Dominion Astrophysics Observatory on Little Saanich Mountain, and his assistants deserve our thanks for giving their time on more than one occasion to the demonstration of the big telescope.

With dinners, dances, teas, garden parties, bridges, and, not last, golf, the social needs of our members were fully catered for. To all concerned in making these functions a success the Association tenders its sincere thanks.

Reference should be made to one or two matters of special interest. With regard to the cancer situation it was felt that for the time being the Association could not do more than reiterate its pronouncement that it had a tentative program drawn up, which it felt would meet the situation, and that it was prepared to carry out any part of this which the financial situation would permit. It was felt, further, that the income to be derived from the funds of the King George Fifth Cancer Campaign was quite inadequate to meet the existing situation, so that a further step forward appears to be imperative if anything worth while is to be accomplished.

With regard to the federation of the various provincial medical Associations with the national body it may be said that the principle has been approved by eight out of the nine provinces. At the Council meeting in Victoria it appeared that there was no doubt that the medical men

across Canada, as represented by the various speakers, were anxious that the profession should be more closely united, in order that their interests might be advanced. It became evident, however, that this movement could not be hurried, for the situations in the various provinces were not identical and certain legal difficulties had cropped up. One difficulty that may be cited was the question of fees, notably in those provinces where a composition fee is payable to cover license to practise and membership in the provincial medical association. This difficulty was overcome, we think satisfactorily, in the case of Alberta, the provincial medical association of which province is now officially "The Canadian Medical Association, Alberta Division". In this particular case an estimate was furnished by the Alberta Division as to how many of the Alberta practitioners were in active work and might desire to receive the *Journal*, and a composition was arrived at on this basis. Another major difficulty in some provinces was as to the legal status of the provincial associations, i.e., whether they would be able to enter into the proposed federation without some enabling and protective provisions. It was therefore felt at Council that a useful purpose would be served by setting up study committees in the various provinces with the hope of developing some plan looking to the fulfilment of federation in a manner acceptable to all concerned. To this end the following resolution was passed:—

THAT each provincial medical association or division be requested to appoint a committee to study federation;

THAT each provincial medical association or division be requested to appoint on its committee at least one member of the Executive Committee of the C.M.A. from that province; and

THAT the provincial committees report, if possible, on or before October 1st, next.

With a view to correlating the work of these nine provincial committees the Executive Committee of the C.M.A. took the following action. Dr. W. K. Colbeck, of Welland, Ont., was appointed chairman of a Sub-Committee of the Executive Committee, to be comprised of one member of the Executive Committee from each provincial association or division, for the purpose of correlating the reports of the study committee of each association or division for submission to the Executive Committee at its next meeting. The following were appointed members of this Sub-Committee: Drs. W. K. Colbeck, Welland, Ont. (Chairman); H. H. Milburn, Vancouver, B.C.; D. S. Macnab, Calgary, Alta.; J. E. Bloomer, Moose Jaw, Sask.; E. S. Moorhead, Winnipeg, Man.; J. C. Gillie, Fort William, Ont.; A. T. Bazin, Montreal, Que.; A. S. Kirkland, Saint John, N.B.; Hon. W. J. P. MacMillan, Charlottetown, P.E.I.; and K. A. MacKenzie, Halifax, N.S.

The Lister Oration was delivered on June 26th by Dr. E. W. Archibald, of Montreal. This

dealt, in the main, with the personal, social and family characteristics of Lister, and broke new ground in a subject that has been rather thoroughly canvassed. A difficult task! Dr. Archibald was listened to with rapt interest and his effort was a worthy contribution to the list of our Orations. His Oration will appear in our October issue.

The Meyers Memorial Prize was awarded to Dr. Ruth MacLachlan Franks, of Toronto, for her essay on "Environment and the Neuroses".

The Osler Scholarships for this year have been awarded to Dr. John G. Howlett, Resident in Medicine, Royal Victoria Hospital, Montreal, and Dr. S. R. Townsend, Senior House Physician, Montreal General Hospital.

Drs. H. S. Birkett, R. D. Rudolf and A. H. Gordon were appointed representatives of the C.M.A. at the Oxford Meeting of the B.M.A.

The new Executive Committee consists of the following members:—

OFFICERS

Chairman—George S. Young, Toronto;
 President—H. M. Robertson, Victoria;
 President-elect—T. H. Legget, Ottawa;
 Hon. Treasurer and Managing Editor—F. S. Patch, Montreal;
 Editor—A. G. Nicholls, Montreal;
 General Secretary—T. C. Routley, Toronto;
 Associate Secretary—G. Harvey Agnew, Toronto.

PROVINCIAL REPRESENTATIVES

Alberta, D. S. Macnab; British Columbia, H. H. Milburn; Manitoba, E. S. Moorhead; New Brunswick, A. Stanley Kirkland; Nova Scotia, K. A. MacKenzie; Ontario, W. K. Colbeck, J. C. Gillie and Duncan Graham; Prince Edward Island, Hon. W. J. P. MacMillan; Quebec, A. T. Bazin, L. Gérin-Lajoie and J. C. Meakins; Saskatchewan, J. E. Bloomer.

Hospital Service Department Notes

Obstetrical Practice in Hospitals

A study of real value to all medical practitioners interested in obstetrics and to all hospitals with maternity facilities has recently been issued by the Council on Community Relations and Administrative Practice of the American Hospital Association. This manual, which was carefully checked by many leading obstetricians in the United States and Canada, outlines the facilities which should be found in every hospital accepting obstetrical patients, and sets forth the regulations and procedures which should govern the conduct of this most important department.

Many valuable recommendations are made. Isolation or segregation accommodation should be available for mother or child; the pre-

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

delivery room should have certain facilities; the delivery room should meet definite requirements, as should also the nursery; equipment should be adequate. The medical staff should be so organized that a high degree of technical procedure can be developed and the work be under the general supervision of the head of the obstetrical service. Prenatal clinics under medical supervision are recommended. An outline is given of what should constitute proper procedures of preparation, delivery, post-partum and follow-up care. The care of the newborn is outlined and a check list of furnishings and equipment for the obstetrical department is included. Copies of this manual may be obtained from the American Hospital Association, of Chicago, for one dollar.

An Unusual Form of Group Hospitalization at Antigonish

Group Hospitalization, or the Periodic Payment Plan for the Purchase of Hospital Care, has been spreading rapidly in the last few years, and while there has been general conformity to certain basic principles the details respecting benefits, premiums and methods of collecting such, have varied widely. In industrial areas it has been possible for the premiums of the members of the plan to be collected by deduction from their pay envelopes, thus simplifying the procedure of collection. Naturally, this is not applicable to a rural area or where other than employed groups are enrolled.

St. Martha's Hospital at Antigonish, Nova Scotia, has met this difficulty of making collections in a rural or non-industrial area by operating through a Cooperative Society. The cooperative movement, which has spread so rapidly in Europe and in many parts of this continent, has many active societies in Nova Scotia, particularly in the Antigonish and Cape Breton areas. Arrangements have been made whereby the Cooperative Society at St. Andrew's, about eight miles from Antigonish, will pay from its dividends and on behalf of its shareholders to St. Martha's Hospital the sum of \$9.00 per shareholder. In return for this premium the shareholders and the members of their families will receive free ward service for an aggregate of five weeks in any one year, free ordinary medicine, and free laboratory service. Patients desiring private or semi-private rooms would receive them at half the usual rate, and the same 50 per cent reduction would be applicable to x-ray service and to operating room charges. Medical care, as in most plans of group hospitalization, will not be included, but will be a matter of arrangement with the family doctor. He, of course, will benefit indirectly, as there will be no hospital account to be met by the patient.

This arrangement would seem to be a very satisfactory one where such cooperative or other community organizations exist. It not only distributes the cost of hospitalization to relieve the burden on the sick individual, but the individual hardly realizes that he is paying a premium at all. Of course, certain considerations would be necessary. The hospital should be assured, as it has been in this case, that the cooperative society is sufficiently sound to meet the premium charges. Moreover, from an actuarial viewpoint, the risk of including families and those who are unemployed is considered to be greater than when membership is limited to employed persons enrolled as groups only. However, these difficulties should be subject to correction or allowance, and should in no way affect the principle underlying this development. It is anticipated that, if the plan proves successful in the St. Andrew's area, the hospital will consider extending the arrangement to other cooperative societies.

Provincial Association Notes

The Prince Edward Island Medical Society

The Prince Edward Island Medical Society held its business session in Summerside on July 10th. The clinical session will be held on September 1st in Charlottetown, so as to coincide with the other Maritime meetings.

An important feature of the meeting was the matter of the affiliation of the Island Association with the Canadian Medical Association. There is a movement to have all the provincial associations merged into one Canadian association on the same lines as the British Medical Association. The general opinion of the meeting was that it was a splendid idea, as a Dominion-wide body would be better able to cope with the various matters that come up from time to time, and that the medical profession would be stronger as a united body than as separate units. There was however the question of finance, as the provincial association would be called upon to bear its share of the cost of affiliation. At present there were only twenty-three out of the sixty practising physicians on the Island affiliated with the Canadian Medical Association.

It was decided that a personal canvass be made by doctors to stimulate interest in other practitioners in the idea of amalgamation. Dr. Keeping was appointed to canvass the doctors in King's County, Dr. MacKenzie in Queen's and Dr. Simpson in Prince. The matter was then laid over to the September meeting. The meeting then adjourned until September 1st, when the Society will meet again at the Canadian National Hotel, Charlottetown, when a clinical program will be arranged with a dinner after-

wards. The President's address will also be delivered at that session. The adjournment was made because representatives from the Canadian Medical Association would be able to be present and address the gathering.

The following officers and committees were elected.

OFFICERS

President, J. W. McKenzie; *Vice-president*, Queen's County, Leo Farmer; *Vice-president*, Prince County, W. B. Howatt; *Vice-president*, King's County, A. W. Ross; *Secretary*, L. B. McKenna; *Treasurer*, I. J. Yeo; *Executive Committee*, Hon. W. J. P. MacMillan, Preston McIntyre, J. A. McPhee, R. D. McNeill, B. C. Keeping. *Canadian Medical Association Council*, Hon. W. J. P. MacMillan, I. J. Yeo, F. J. McNeill, J. E. Johnson, A. A. McDonald. *Auditors*, J. A. McPhee, E. S. Giddings. *Editorial Board of Canadian Medical Association Journal*, J. F. Dewar, Hon. W. J. P. MacMillan.

COMMITTEES

Public Health, Hon. W. J. P. MacMillan, B. C. Keeping, W. B. Howatt, G. L. Smith, R. Kennedy. *Entertainment*, W. Tidmarsh, J. D. McGuigan. *Constitution and By-laws*, H. D. Johnson, E. T. Tanton, J. C. Simpson. *Credentials and Ethics*, G. F. Dewar, J. B. Champion, J. E. Fleming. *Economics*, R. F. Seaman, H. W. Moyse, D. Campbell. *Maternal Welfare*, Hon. W. J. P. MacMillan, W. Tidmarsh, J. C. Simpson. *Medical Education*, I. J. Yeo, J. A. McPhee, J. C. Houston. *Pharmacology*, J. W. Keir, M. Delaney, W. H. Soper. *Cancer Study*, Hon. W. J. P. MacMillan, R. F. Seaman, E. T. Tanton. *Prince Edward Island Medical Council*, J. F. McNeill, Hon. W. J. P. MacMillan, G. F. Dewar, I. J. Yeo, H. D. Johnson, R. F. Seaman, J. A. McPhee.

J. W. MCKENZIE, *Secretary*.

Medical Societies

Ontario Neuro-Psychiatric Association

The Annual Meeting of the Ontario Neuro-Psychiatric Association for the year 1936 was held at the Ontario Hospital, Brockville, on Friday, June 19, 1936. The Ontario Association was host to the psychiatrists of the Province of Quebec and their wives, and the meeting saw an interchange of views by the doctors of the two provinces.

The President, Dr. G. C. Kidd, Medical Superintendent of the Ontario Hospital, Cobourg, was in the chair and the welcome was extended by Mayor Comstock, of Brockville. There were several papers and discussions at the sessions. Dr. E. H. Kinsman of the Ontario Hospital, Toronto, and Dr. A. M. Doyle of the Ontario Hospital, Kingston, presented case reports. Dr. C. H. McCuaig and Dr. Trevor Owen gave a symposium, "Difficulties in differentiating between hyperthyroidism and anxiety states", which was led in discussion by Dr. Colin K. Russel of Montreal. Dr. Daniel Plouffe, Medical Superintendent of Bordeaux Hospital, Bordeaux, Quebec, gave a paper on the "Attitude of the psychiatrists as experts in criminal

courts". Dr. C. A. Porteous, Superintendent of Verdun Hospital, Montreal, led the discussion. Dr. Grant Fleming, Professor of Public Health and Preventive Medicine at McGill University was the speaker at the informal Association dinner.

The following officers were elected for the coming year: *Honorary President*, The Hon. Dr. J. A. Faulkner, Minister of Health for Ontario. *President*, Dr. G. H. Stevenson, Superintendent, Ontario Hospital, London. *Vice-President*, Dr. J. P. Cathcart, Chief Neuro-psychiatrist of the Department of Pensions and National Health, Ottawa. *Secretary*, Dr. A. McCausland, Ontario Hospital, London.

A. MCCAUSLAND

Post-Graduate Courses

The Montreal Medico-Chirurgical Society will hold its Fourth Annual Clinical Convention in conjunction with the Reunion of Graduates of McGill University, on October 21 to 24, 1936.

Interesting and varied clinical sessions are being planned by the Program Committee. These sessions will be held in the Royal Victoria Hospital, the Montreal General Hospital, the Royal Victoria Montreal Maternity Hospital, the Children's Memorial Hospital, and McGill University, and will run continuously on the above dates.

The New York Academy of Medicine

For the Annual Graduate Fortnight of the New York Academy of Medicine a subject of outstanding importance in the practice of medicine and surgery is selected and is presented from as many angles as possible. An attempt is made to offer to the profession a grasp of the advances in medicine so that the busy practitioner may be informed as to the last word on a given topic.

The Ninth Annual Graduate Fortnight will be held October 19th to 31st and will be devoted to a consideration of Trauma; Occupational Diseases and Hazards.

Twenty-three important hospitals of the city will present coordinated afternoon clinics and clinical demonstrations. At the evening meetings prominent clinicians from various parts of the country who are recognized authorities in their special lines of work will discuss various aspects of the general subject.

A comprehensive exhibit of books, pathological and research material, apparatus for resuscitation and other first aid appliances will be assembled. Demonstrations will be held at regular intervals.

Some of the features to be presented at the meetings, in the clinics and in the exhibit

will be: First aid in industry, in the home and on the highway; Accidents and their management; Resuscitation; Shock and hæmorrhage; Hazards in athletics; General principles of fracture treatment; Fractures of the extremities; Injuries of the head, spine, abdomen, chest and genito-urinary systems; Hand injuries; Burns—thermal, electrical, radiant and chemical; Medico-legal aspects of trauma and disability; War injuries and emergencies including—injuries caused by high explosives, medical aspects of chemical warfare, gas attack, gas defense; Carbon monoxide poisoning; Fatigue and noise in industry; Harmful conditions in industry; Occupational diseases; Occupational hazards; Industrial poisonings; Relation of trauma to disease.

The medical profession is invited to attend. A complete program and registration blank may be secured by addressing: Dr. Frederick P. Reynolds, the New York Academy of Medicine, 2 East 103rd Street, New York City.

St. Michael's Hospital, Toronto

The annual post-graduate week of lectures and clinics will be held at St. Michael's Hospital, Toronto, as usual, during the week following the Canadian National Exhibition, September 14th to 19th inclusive. The course is free to all graduates in medicine. For further particulars please write Dr. W. B. Edmonds, Medical Arts Building, Toronto.

The Second International Medical Week in Switzerland

This "Week", organized by *Le Journal Suisse de Médecine* under the patronage of the Supreme Swiss Federal Council, will be held at Lucerne, Switzerland from August 31st to September 5th.

The subjects to be considered are: General Questions in regard to Circulation, Respiration, Tuberculosis; Nutritive Metabolism; Pædiatrics; Intoxications; Clinical Cases.

The following persons are announced to take part. R. Bing, Bâle; P. Clairmont, Zurich; P. Decker, Lausanne; G. Frontali, Padua; J. Fulton, Yale University, New Haven, U.S.A.; E. Gäumann, Zurich; R. Grégoire, Paris; Freiherr F. v. Gröer, Lwow, Poland; H. Guggisberg, Bern; J. A. Gunn, Oxford; C. Henschen, Bâle; W. R. Hess, Zurich; W. Heubner, Berlin; H. C. Jacobaeus, Stockholm; W. Löffler, Zurich; E. Mellanby, London; O. Naegeli, Zurich; M. Péhu, Lyons; E. P. Pick, Vienna; F. Rathery, Paris; M. Roch, Geneva; F. Sauerbruch, Berlin; Ph. Schwartz, Istanbul; A. Szent-György, Szeged; A. Vogt, Zurich; L. K. Wolff, Utrecht; Hch. Zangger, Zurich.

Communications may be addressed to the Secretariat of the Second International Medical

Week in Switzerland, Klosterberg 27, Bâle, Switzerland, from which all information may also be obtained.

Special Correspondence

The London Letter

(From our own correspondent)

After many years of discussion and various special committees on the reform of the medical curriculum the General Medical Council has now crystallized the whole matter by passing resolutions to come into force in January, 1938. In most ways the proposed changes are all to the good and in particular during the three clinical years there are grounds for hope that all the essential subjects will now be taught in proper relationship to each other. The two pre-clinical years appear to be somewhat overcrowded, for the introduction of genetics, psychology and elementary clinical methods here has not been balanced by much deduction of the time spent on existing subjects. Overloading by anatomy still seems to be open to serious criticism. However, more stringent comments are being made of a still earlier part of the curriculum, namely, the pre-registration regulations. Here there seems to be some confusion and no guarantee that the strong demand from all quarters for a better general education has been met satisfactorily. Reports of the actual discussion at the General Medical Council meeting and subsequent correspondence in the medical press suggest that the new regulations represent a regrettable retrograde step. A new examination is introduced in a general subject *only* for those who attempt to take their preliminary part of the medical course before entering a medical school. Thus a new principle is introduced which seems to put the public schools in a different position and which is roundly called a "breach of faith" in some quarters. There is still time for the General Medical Council to put the matter right if the new resolution means what it is taken to mean.

The use of psychological methods for the selection of candidates for industrial occupation is gaining ground although still viewed with suspicion by "big business". A recent report of the Industrial Health Research Board brings out points of great importance. For example it is clearly proved that intelligence tests could with advantage be adopted in the selection of candidates for highly skilled work but are of no value where the occupation is of a routine type of a simple kind. It also seems to be proved that psychological tests not only have a prognostic value during the learning period but actually correlate closely with the degree of proficiency shown when maturity has been reached. A striking practical application of tests for vocational guidance on a big scale has

recently been recorded with reference to the selection of apprentices for training as aircraft engineers in the Royal Air Force. By a study of the after-careers of apprentices tested in 1932 it is shown that had the results of the tests been used in their selection there would, in fact, have been a considerable saving in public money, for about 10 per cent of those trained who failed to reach the higher grades in their final tests would not have been selected. In other words selection by special tests would have produced the same number of the higher grade men from a smaller number of apprentices.

Recent work on puerperal sepsis has made important advances in two directions. On the one hand the use of new synthetic dyes appears to offer a hopeful line of attack upon infections caused by the hæmolytic streptococcus. Even more important work has been carried out especially at the Queen Charlotte's Hospital Research laboratories on the prevention of puerperal infection. It seems clearly shown that it is in the throats or noses of the human personnel around the newly-delivered mother (or even her own) that a large amount of danger lies. Dr. Leonard Colebrook follows up his previous publications on this subject by a strong call to action. An organized system of throat swabbing, it is claimed, could be used to secure that dangerous sources of infection were not allowed near a maternity case and further a plea is made for a definite policy with regard to instruction in the use of masks and the most effective antiseptic precautions.

Notes have been made from time to time in these letters on the vexed question of malnutrition among the children of this country. Now an enterprising medical officer of health has set about finding out not what food was available for children but what in fact they did eat. All the children attending certain elementary schools were asked to write down what they had eaten for breakfast, dinner, tea, and supper on Tuesday, September 17th, and on Tuesday, December 10th, 1935. Each meal was recorded on a separate piece of paper, and neither the name of the child nor the school was given. The children were not informed of the reason for this request, and in an endeavour to remove any competitive element from the recording of meals the proposition was put to the children as a memory test. On Tuesday afternoon they were asked to write down what they had had for breakfast and dinner on that day, and on the Wednesday morning they recorded what they had eaten for tea and supper on the previous day. The results show that milk, soup, eggs, fish, cheese, fruit, vegetables, and pudding do not appear in the diet as frequently as is desirable. Even if allowance is made for milk which is consumed in varying quantity with tea, coffee, cocoa, and cereals the position is far from satisfactory. "Tea" and "bread-and butter" each form part of 70 per cent of breakfasts; "tea and meat and potatoes"

about 60 per cent of dinners; and "tea and bread-and-butter" over 70 per cent of teas. Many of the children have a light meal in the middle of the day and their chief meal is tea—the familiar high tea so common in industrial areas. Supper is a variable meal but the consumption of a heavy meal before going to bed was recorded much more frequently than was anticipated.

ALAN MONCRIEFF.

121 Harley St.,
London, W.1.

The Edinburgh Letter

(From our own correspondent)

The reputation of Aberdeen University as a medical school has never stood higher than it does at the present time. This reputation will be enhanced when the new Royal Infirmary at Foresthill at present under construction is completed. The hospital will accommodate 500 patients and embodies the most modern features in design and equipment. The most careful consideration has been given to every detail connected with the lay-out of the hospital and this should result in great convenience and efficiency in working. A deputation from the Westminster Hospital London, which is to be rebuilt at a cost of £750,000, recently paid a visit to Aberdeen to see what will undoubtedly be one of the finest hospitals in this country.

The hand-writing of doctors is very frequently the subject of witticisms on the part of the public and possibly with very good reason. The use of the typewriter has to some extent made things easier for those who had laboriously to decipher his epistles. The legibility of prescriptions is still however a source of complaint. This matter was recently before a meeting of the Glasgow Insurance Committee as the result of a complaint by a chemist that in a number of prescriptions it was quite impossible to decipher some of the items and that in consequence delay was caused to the patient and trouble and expense to the dispenser on account of the necessity for ascertaining from the doctor what was really intended. The Committee decided to request the culprit to give an assurance that in future he would write his prescriptions legibly. Had this occurred in Norway it is possible that the doctor would have been more severely dealt with as in that country the illegible writing of prescriptions is a punishable offence.

The death has occurred in Edinburgh of Dr. Hamilton Marr who retired in October last from the office of Senior Commissioner of the Board of Control. He was formerly Medical Superintendent of the Glasgow District Asylum, Woodilee. He was a lecturer in Psychological Medicine in St. Mungo's College, Glasgow, and extra-mural lecturer on Mental Diseases in Glasgow University. During the War he was specialist in nervous diseases to the troops in Malta and later

consultant in mental diseases to the Scottish Command. He was an Honorary Lieutenant-Colonel in the R.A.M.C., and in 1932 he received the Order of C.B. His publications included "Psychoses of the War—including Neurasthenia and Shell Shock", "The Feeble-Minded", and various articles in medical journals.

In the Annual Report of the Department of Health for Scotland for 1935 it is noted that the building of houses by Local Authorities—18,651—was the highest ever achieved. The number of houses built with State aid since 1919 has now reached a total of 200,284. The infantile mortality rate for the year was 76.8 per 1,000 births which is again the lowest on record, though the Department considers that this rate is still too high. The number of women who died during the year from causes peculiar to pregnancy and child-birth was 554, the maternal mortality rate being 6.3 per 1,000 births. In this connection it should be noted that the Secretary of State for Scotland is to introduce a Maternity Service Bill in the House of Commons during the current session. Dealing with the National Health Insurance Service the report shows a substantial increase in the number of notified cases of completed incapacity compared with the previous year. Over 395,000 insured persons were incapacitated during the year and the days of incapacity numbered over 18,500,000. The increase is mainly attributed to an influenza epidemic in the spring of 1935. Several sharp outbreaks of enteric fever were an unusual feature during the year. The main outbreaks were due to food infection. The principal causes of death were heart disease, malignant tumours, cerebral hæmorrhage, pneumonia and tuberculosis. Improved diagnosis has tended to increase the number of deaths attributed to malignant disease but there can be no doubt, the Report states, that the steady upward trend of deaths from this cause constitutes a challenge to medical science. It should be noted that the Scottish hospitals are taking a prominent part in developing facilities for early diagnosis and treatment.

R. W. CRAIG.

7 Drumsheugh Gardens,
Edinburgh.

Yes, I can see and envy not
The Sardinian monarch's wealthier lot;
I care not for his state and treasure,
Grandeur for me has nought of pleasure.
I'll bathe my head with perfumes now,
With roses bind my laughing brow.
I'll live today and banish sorrow,
For who can tell he'll live tomorrow?

—Anacreon.

Topics of Current Interest

Physical Education

The year 1935 will be a memorable one in the history of physical education in this country. The prominence given to physical fitness by the King's Jubilee Trust Fund has stimulated official and voluntary organizations concerned with gymnastics and games for children and young people to greater energy, while the need for recreative and enjoyable occupation for unemployed men and women in distressed areas has led to the setting up of schemes for physical training which, it is hoped, will be developed and extended to the great benefit of national health and physique. Physical training has been slow to receive adequate recognition in England. It first became a normal and regular part of the elementary school curriculum in 1909. Sir Robert Morant, then secretary of the Board of Education, realized not only its importance to the health of the growing child, but its close association with the school medical service and hygiene. Therefore he entrusted the preparation of a revised syllabus of physical exercises to the medical department of the Board, and placed the newly appointed staff of special inspectors under the general control and guidance of Sir George Newman. The progress of physical education may be read in the successive reports of the chief medical officer. A new syllabus was called for in 1919, and yet another in 1933; from time to time supplementary matter has been issued dealing with particular problems such as the organization of games, the work in small country schools, the value of playing fields, and so forth; and there are other books now in preparation which will provide for the needs of the older boys and girls in the senior schools.*

The general policy of the Board of Education has been to leave physical training in the elementary schools in the hands of the class teachers; to give all teachers some special training, but to encourage them to supplement this by attendance at suitable vacation courses and classes; and to support the appointment by local education authorities of expert organizers whose duties include general supervision of physical training and advice to individual teachers. This policy has been successful, but it is pleasing to note that the Board now appear to be pursuing it with greater energy, and that increased attention is being paid to secondary education in this subject. Systematic physical training, as apart from games, has been seriously hampered in public and secondary schools for boys by the lack of trained gymnastic masters; even now there is only one training

* See the report of the C.M.O. of the Board of Education for the year 1934. H.M. Stationery Office. 2s. 6d.

college for men—viz., Carnegie Hall, founded at Leeds a few years ago by a grant from the Carnegie United Kingdom Trust—whereas for 50 years there have been facilities for the training of women. Fortunately the growing demand for teachers and “leaders” is bound to result in more ample opportunities for training, as well as greater scope for employment after qualification. But the authority of the Board is limited to schools and educational work, and there is a strong feeling that much more might and should be done for the promotion of physical activity in its broadest sense, not only among young men and women, but among older persons of both sexes. The “keep fit” movement, for example, which originated in Sunderland and is rapidly spreading over the whole country, is providing healthy physical interests for hundreds of women, many of mature age, who had never experienced the joy of movement before. Gymnastic classes and games are doing the same for young men. The Central Council of Recreative Physical Training, a representative and voluntary organization established early last year under the patronage of the King and Queen and the presidency of Lord Astor, has been formed to coordinate and encourage all types of recreative activity. The national playing fields association, organization for the promotion of athletics, swimming, camping, hiking, as well as games, dancing, and gymnastics, are all combining to arouse a much wider appreciation of the value of exercise, open air, and sunshine, and to show that no one need feel too old or too stiff to enjoy some form of exercise.

In this country we have long been proud of our traditional games, though they have been played by the few rather than the many. Our system of gymnastics was borrowed mainly from the Scandinavian countries. But at long last we are beginning to develop a scheme of physical education of our own, which we hope will be characteristically national. We shall take full advantage of the experience and knowledge of other lands, but shall adopt, modify, and add to this so as to meet the needs of our climate, our social and educational conditions, and our national habits and customs. Physical education, wisely used, has an immensely important contribution to make towards a state of positive good health, which is something much better than the mere prevention of disease.—*The Lancet*, 1936, 1: 93.

Corpse Blood for Transfusion

It is now the practice at a large hospital in Moscow to obtain blood for transfusion from patients brought in dead. The method used and the physiological facts on which it depends offer several points of interest. The method and its results are described in a recent paper

by Judine,* who acknowledges an indebtedness to his colleagues Skoudina and Roussakov for their observations on the behaviour of the blood after death. In healthy subjects dying suddenly the blood is said to coagulate rapidly, only to undergo deocoagulation or, as it is termed, “fibrinolysis”, within the next hour, after which it remains permanently incoagulable. This fact alone constitutes an advantage over blood from a living donor, since no addition of an anti-coagulant or, alternatively, abstraction of fibrin is necessary. The best type of subject is one who has died from coronary disease or electrocution, and the method of obtaining the blood is to open the jugular veins and place the body in the Trendelenburg position; the yield of about 3 litres is derived from the systemic circulation only, and is usually found to be sterile. A subsequent post-mortem examination on the donor as well as the necessary tests applied to the blood itself establish its suitability for use, and it can then be stored in the cold for periods of up to three weeks. Such blood is said to be less apt to cause reactions than blood from living donors, and it has a further advantage in the fact that repeated transfusions of the same blood can be given, instead of using the blood of several different living donors. Nearly one thousand transfusions of blood from the cadaver have been given in Moscow with eminently satisfactory results, and the method has evidently come there to stay. The organization of such a transfusion “service” is, of course, only possible in an institution receiving large numbers of fatal casualties, from among which the most suitable donors can be chosen. It has a more formidable drawback in the sphere of sentiment, and although convenience and economy may weigh heavily on the other side of the scale, we can hardly picture the method being adopted in this country.—*Brit. M. J.*, 1936, 1: 894.

* *Presse Méd.*, 1936, 44: 68.

My soul, what's lighter than a feather? Wind.
Than wind? The fire. And what than fire? The mind.
What's lighter than the mind? A thought. Than thought?
This bubble world. What, than this bubble? Nought.

My soul, sit thou a patient looker-on;
Judge not the play before the play is done;
Her plot has many changes; every day
Speaks a new scene; the last act crowns the play.

—Francis Quarles, Epigram 15.

Abstracts from Current Literature

Medicine

Non-Spirochætal Infectious Jaundice. Bates, R., *Brit. M. J.*, 1936, 1: 521.

The author records observations on an epidemic of 65 cases of infectious jaundice occurring in a colony for mental defectives. He notes that in England infectious jaundice occurs in two forms—as Weil's disease, severe, and spirochætal in origin, and, as in this epidemic, in a mild form, the cause of which is unknown. While sporadic cases of catarrhal jaundice may be instances of gastro-duodenal catarrh with blockage of the ducts, it is probable that many sporadic as well as the mild epidemic cases represent instances of infective hepatitis. Bacteriological work on the blood, urine and fæces in this epidemic was essentially negative. Of the 65 patients, 27 were under 10, 47 under 15, and only 6 over 25 years. Some cases set in with sore throat, suggesting a possible nasopharyngeal portal of entry for the virus. Malaise, headache and abdominal pain were usual initial symptoms. In a few cases right iliac fossa pain was prominent. In the younger patients an early sign was conjunctival injection. In 28 cases jaundice appeared with the onset symptoms, while 21 cases had a pre-icteric febrile period of 1 to 11 days, and 6 cases were non-icteric. Initial temperatures to 103° were usual. Jaundice lasted more than 1 week in 16 cases and over 2 weeks in 4. Pale stools for 24 hours were common. The liver was usually considerably enlarged; the spleen, definitely so in 10 cases. Albuminuria was present in 11 cases. Vomiting was uncommon. Acidosis however was quite a prominent feature, probably the result of the carbohydrate-fat metabolism derangement due to the hepatitis.

Definite evidence of contact infection was of course obtainable, and the incubation period was established as from 15 to 21 days in the younger patients, and usually 26 days in the older. It is recommended that every case of "catarrhal" jaundice in children be isolated for at least four weeks, since any single case may be the start of an epidemic, especially in institutions. Treatment should be largely directed to the acidosis, and the early institution of carbohydrate and alkali therapy appears to shorten the duration of jaundice.

W. FORD CONNELL

Glycosuria of the "Lag Storage" Type—an Explanation. Lawrence, R. D., *Brit. M. J.*, 1936, 1: 526.

This type of glycosuria, first described by McLean, has up to the present never been satisfactorily explained, nor has its significance been properly established. Individuals exhibiting it show no symptoms, but are found on

routine examination to exhibit glycosuria fairly constantly after meals containing rapidly soluble carbohydrate. Investigation reveals that their fasting blood sugar is always normal, but that the ingestion of 50 grams of glucose is followed in half an hour by a rise of the capillary blood sugar level to 0.25 or 0.3 per cent. This falls rapidly, being still above the renal threshold at one hour, so that the half and one hour specimens of urine show much sugar. Within two hours, the blood sugar has dropped to or below the fasting level. (This curve is not well shown on venous blood, which explains the comparatively infrequent recognition of this condition in America and Canada). The author has frequently observed the development of this condition following gastro-enterostomy and in cases of duodenal ulcer, and has simulated the curve in normal persons by giving them glucose by a duodenal tube. He considers that patients showing the curve have absolutely no defect of carbohydrate metabolism, the condition being due solely to unusually rapid intestinal absorption of sugar, so that the storage mechanism of the liver, muscles and tissues cannot keep pace. Whereas from 5 to 10 per cent of normal persons have a low renal threshold for sugar, i.e., show renal glycosuria, the author believes that about 2 per cent show the above type of blood sugar curve. The term "lag storage curve" could hardly be more misleading, and the author prefers to call the condition "oxyhyperglycæmia", i.e., "sharp" or "steep" hyperglycæmia, a term which accurately describes the condition.

W. FORD CONNELL

Pneumococcus Type III Pneumonia. An Analysis of 500 Cases. Cecil, R. L., Plummer, N. and McCall, M., *Am. J. M. Sc.*, 1936, 191: 305.

The authors point out that pneumococcus type III ranks third as an exciting agent in lobar pneumonia, causing 11.8 per cent of all pneumococcal pneumonias. Its incidence increases with age and is more common in women than men. It is prone to occur in those who are already the victims of some chronic disease. In their series of 500 cases 49.9 per cent of the patients were afflicted with some chronic malady. Bacteriæmia occurred in 29.4 per cent of cases subjected to blood culture. The death rate was 42.2 per cent of all cases; in 85.4 per cent of the bacteriæmic cases. The disease has been treated with homologous convalescent serum without success. Transfusions from persons vaccinated against type III pneumococcus have likewise failed. Vaccination as a prophylactic measure has been unsuccessful. Polyvalent pneumococcal vaccine administered subcutaneously will produce in the serum a high titre of agglutinins and protective bodies for type I and type II, but no protection against type III. The authors conclude that there is no satisfactory serum therapy

for pneumococcus type III. The most promising outlook with respect to specific treatment is the enzyme of Avery which destroys the specific carbohydrate in the capsule of the type III pneumococcus. Already this enzyme has shown distinctly curative properties in the case of animals infected experimentally with lethal doses of the type III pneumococcus. It is produced by a motile spore-bearing pleomorphic bacillus isolated from peat oil by DuBois and Avery.

E. S. MILLS

Surgery

The Surgery of Jaundice. Walton. Sir J., *Brit. M. J.*, 1936, 1: 979.

Jaundiced patients are toxic, have to be carefully prepared, and the time cautiously selected, for operation. Carcinoma of the pancreas is the commonest growth of the pancreas. It may be primary or secondary. It affects both sexes equally. The patients are generally over middle age. The characteristic history is short; constant pain, progressive jaundice passing to a grey-green colour, absence of bile in the stool, a firm liver, and a dilated gall bladder being noted.

Acute pancreatitis rarely is associated with jaundice. Three groups of chronic pancreatitis are recognized: (1) with predominant gastric symptoms; (2) with obstruction to common duct; and (3) the type producing diabetes. In over half jaundice is a dominant symptom. Differential diagnosis is often difficult. Jaundice is usually steadily progressive. There may be a premonitory attack. The history is longer in jaundice due to chronic pancreatitis. Differentiation may be impossible at operation. Cholecystgastrostomy or cholecystoduodenostomy is the treatment of choice. Rarely, a localized carcinoma may be excised.

Carcinoma of the bile ducts is a relatively rare cause of obstructive jaundice. It rarely develops in the cystic duct. Symptoms and signs vary somewhat according to the situation of the growth. Usually a palliative cystoduodenostomy or cystogastrostomy only is possible. Rarely the growth can be excised and the duct reformed. Congenital dilation of the common bile duct is a rare condition. Over 90 per cent of cases are found in females. Symptoms are periodic at first, later, more constant. Characteristic signs and symptoms are pain, jaundice, and the presence of a tumour. The ideal treatment is choledochoduodenostomy. If the patient is very ill temporary drainage should be done. The commonest cause of stricture of the common duct is technical accident. Ulceration from a stone is a rare cause. The four common methods of injuring the common bile duct are (1) mistaking the common bile duct for the cystic when traction is exerted on the gall bladder, (2) attempting to retrieve a bleeding cystic artery blindly, (3) adhesions between cystic and

common hepatic ducts obscuring the arrangement, and (4) adhesions between the pouch of Hartmann and the common bile duct obscuring the arrangement. Some form of reconstruction is necessary. This is technically difficult.

Stones in the common duct result in attacks of colic with obstruction and jaundice. These are closely associated in point of time. Rigors indicate an associated cholangitis. Loss of weight may be marked. The jaundice rarely becomes grey-green. Itching may be present. Diagnosis is not always easy. At operation the diagnosis is first confirmed. The gall bladder is removed. The common duct is opened by enlarging the cystic duct. Stones are then removed. The forceps should be passed into the duodenum. If pus is present the duct should be drained; if not, then the opening should be sutured and a drain placed down to it.

Hæmolytic jaundice is present in pernicious anæmia and acholuric jaundice. Operation is rarely, if ever, considered in the former. The latter can be cured by splenectomy. Pigment stones in the gall bladder shortly give rise to cholecystitis. If the patient's condition persists a cholecystectomy should also be done.

STUART GORDON

Shock: The Mechanism of Death following Intestinal Obstruction. Moon, V. N. and Morgan, D. R., *Arch. Surg.*, 1936, 32: 776.

The mechanism by which death results from intestinal obstruction remains a debated question. There is a similarity between shock of various origin in man and experimental shock and the phenomena resulting from intestinal obstruction. A characteristic group of symptoms is produced in dogs when shock is induced without trauma and without the complicating factor of deep narcosis. By introducing freshly finely chopped dog muscle into the peritoneal cavity, by the intravenous injection of peptone, of watery extracts of various tissues or histamine, the animal becomes inactive and listless and refuses food. There are muscular tremors, vomiting, salivation and, in the later stages, the passage of bloody, fluid stools. The pulse becomes rapid, the blood pressure falls, the temperature becomes subnormal or sometimes increased, and the respirations are slow and deep. The urine becomes scanty and concentrated. Coma and evidence of failure precede death. Most of the studies on intestinal obstruction were published before it was recognized that shock is accompanied by characteristic changes, demonstrable by post-mortem examination.

Hæmorrhagic manifestations have been noted in the intestines, lungs, liver, and kidneys. The fact that the spleen does not usually share in the visceral congestion is significant. The spleen acts as a reservoir for food not needed in the system. Shock is similar to hæmorrhage in its

effects, and the spleen discharges its reserve of blood in a physiological effort to meet the systemic demand. Occasionally, the authors found the spleen relaxed and enlarged, but usually it is contracted dry, and bloodless. A decrease in blood chloride is not a distinctive feature of intestinal obstruction. It is met in other conditions terminating in circulatory disturbances of shock type. The same applies to the high non-protein nitrogen content of the blood. The extract of obstructed mucosa used in the authors' experiments was much more potent than that of normal mucosa under like conditions. The combined effects of histamine, products of disintegration of tissue and products of bacterial activity, any one of which alone will produce shock, will account for the clinical manifestations and post-mortem observations in cases of intestinal obstruction or strangulation, whether occurring spontaneously or experimentally.

G. E. LEARMONTH

Obstetrics and Gynæcology

Trichomonas Vaginalis. Collis, J. L., *J. Obst. & Gyn. Brit. Emp.*, 1936, 43: 87.

The trichomonas is a flagellated protozoon, first described in 1837 by Donne, which causes a rather acute vaginitis, characterized by profuse yellowish-white, thin discharge and a great deal of itching of the vulva. The vaginal lining, particularly in the posterior fornix, becomes reddened and oedematous with white points dotted all over it. There are many theories as to the source of this infection, such as that it originates from the bowel, the mouth, water, etc., but none of them seem very satisfactory. The author believes that the trichomonas travels as spores, lodges in the vagina, but only sets up an infection when the resistance of the vagina is lowered by general or local disease.

The treatment which has been found most efficacious is the use of "Devegan" tablets. This treatment is based on the fact that not only are the organisms killed, but the breaking down of glycogen is arrested and so the vaginal wall restored to normal. Two tablets are inserted each day at the start, for six weeks. Within 24 hours no trichomonas can be found in smear examination. The treatment is then modified to one tablet a week, the average duration of treatment being 3 months.

ELEANOR PERCIVAL

Blood Chemistry and Renal Function in Abruptio Placentæ. Dieckmann, W. J., *Am. J. Obst. & Gyn.*, 1936, 31: 734.

Patients with abruptio placentæ may be divided into a toxæmic hypotensive or vascular disease group and a non-toxæmic group. In the former the majority of the cases are associated with a persistent hypertension, which may have been initiated and intensified by the pregnancy

rather than with a true pre-eclampsia and eclampsia. The non-toxæmic group is associated with local conditions in the uterus. These may be subinvolution due to multiparity or infection, abnormal implantation, faulty contractions of the uterus, etc. The hæmoglobin, hæmatocrit and serum protein concentrations are lowered proportionately to the hæmorrhage. If the loss of these substances is great enough death may occur as a result of tissue anoxæmia and improper interchange of water and electrolysis. The determination of the hæmoglobin and serum protein concentration on admission does not, as a rule, give a true index of the volume of the hæmorrhage or of the patient's condition. The systolic blood pressure on admission may be 100 mm. or more and yet the patient may be in shock. The blood fibrin may also be reduced to a concentration which predisposes to bleeding from mucous surfaces, incisions, and the uterus. The renal function is impaired in many cases but returns to normal after an interval of several months. These tests demonstrate that a chronic nephritis is not present. The prevention or cure of the associated phenomena is the prompt, adequate, and conditioned administration of blood and parenteral fluids.

ROSS MITCHELL

Anæsthesia

Local Anæsthesia in Minor Surgery. Abel, A. L., *The Practitioner*, 1936, 136: 509.

There is a definite place for the use of local anæsthesia and it is especially indicated for the painless performance of lumbar puncture, blood transfusion, the removal of small growths, endoscopic examination of the œsophagus, bronchi, urethra and bladder, etc. In these cases the use of a general anæsthetic is rarely, if ever, justified. Two types of local anæsthesia are in general use: (1) those which produce their effect by freezing the tissues, and (2) those which induce anæsthesia by chemical action on the nerve. Ethyl chloride is the classical example of the first group. The outstanding members of the second group are cocaine, novocaine and nupercaine (percaine). Cocaine has been largely replaced by nupercaine, which is far less toxic and long outlasts its anæsthetic effect. Novocaine is suitable for minor operations of short duration. The advantages of a local anæsthetic are that it allows the surgeon to work single handed, and the patient is saved the inconvenience and possible risk of a general anæsthetic. It is contraindicated in the presence of sepsis. The disadvantages are an apprehensive patient and increased mental anxiety of the surgeon when operating upon a conscious patient.

The indications of use include (1) surface applications to mucous membranes, (2) by injection, (3) in the treatment of recent open

wounds; and (4) for the relief of pain. Surface anaesthesia is employed in the surgery of the eye and in oto-rhino-laryngology. Nupereaine is a complete substitute for cocaine which has been used so long in these fields.

By injection is meant the use of local anaesthetics either as an infiltration process or as a nerve block. A more recent use is to deposit an anaesthetic solution between the broken ends of bone in a fracture preparatory to reducing it. In the treatment of recent open wounds the most effective sterilizing solution is 1 in 20 carbolic acid. If this is applied to a recent wound over its whole area for five minutes, not only will complete sterilization be assured, but local anaesthesia also takes place. The wound should now be excised and a similar solution re-applied for a further five minutes. The wound should then be sutured completely and primary union will occur. [Abstractor's Note: Compare with the novocaine pack: Contribution to the therapy of fresh accidental wounds, by M. Fritz and E. K. Tanner, Brooklyn, *New York State Journal of Medicine*, 1935, 35: 1217.]

Local anaesthesia finds a useful application in the treatment of intractable pain. Alcohol injection for trigeminal neuralgia and as a treatment for Raynaud's disease and thrombo-angiitis obliterans (Buerger's disease) is a good example of this.

ARTHUR WILKINSON

Therapeutics

Bacterial Meningitis — A Comparative Study of Therapeutic Measures. Tripoli, C. J., *J. Am. M. Ass.*, 1936, 106: 171.

Presenting a study of 468 cases of bacterial meningitis, the author critically considers the results obtained with varied therapeutic measures. Of this series 221 were acute cerebrospinal meningitis. The mortality rate was 65 per cent. Six different modes of therapeutic attack are described, varying from simple lumbar drainage to combined punctures (ventricular or external) with the lumbar tap. This, combined of course with the intensive use of antisera. In the remaining group, *i.e.*, those with other causal organisms, the mortality figures reached the appalling figure of 98.3 per cent, with similar types of treatment.

The author's summary is pessimistic to a degree and leads to no definite conclusion as to the relative merits of the different therapeutic methods. There is some suggestion that cisternal puncture is of value, but its dangers seem almost to preclude its use. The use of antiseptic chemical agents has proved of little value. The only slight positive indication in the series excluding the cerebrospinal fevers, was the recovery of 4 cases under spinal lavage with non-specific antisera and eradication of the primary focus. The author's final statement that the

treatment of bacterial meningitis is unsatisfactory seems conservative to a degree.

G. N. PATERSON-SMYTH

Nervous Complications Following Spinal Anaesthesia. Broek, S., Bell, A. and Davidson, C., *J. Am. M. Ass.*, 1936, 106: 441.

The rapidly growing use of cocaine derivatives intraspinaly has given rise to certain interesting and important considerations. It has been clearly demonstrated that there are, at times, very definite toxic effects on the nervous tissue which would tend to make one clearly realize that the procedure is not devoid of danger. Many descriptions of neurological sequelae are to be found in the literature, but authorities differ widely as to the frequency of occurrence. Hyslop gives 0.5 per cent and Jarman 0.01 per cent, while Foss and Schwalm have seen no nervous sequelae in 3,000 cases.

The present authors then present seven cases. These range from benign aseptic meningitis to polio-encephalitis and toxic myelopathy with a fatal termination. All these patients had been injected with various cocaine solutions, nupercaine, procaine, etc. The only explanation that can be advanced is some form of tissue sensitivity on the part of the patient. In six of the cases a direct chemotaxic effect seems evident, though this is far from a complete explanation. The conclusion drawn is that in view of the impossibility of detecting such tissue sensitivity, the use of spinal anaesthesia should be employed with considerable caution. G. N. PATERSON-SMYTH

The Intensive Treatment of Morphine Addiction. Klingman, T. and Everts, W. H., *J. Am. M. Ass.*, 1936, 106: 1.

Pointing out the striking differences in the personality make-up of addicts the authors describe a method of intensive treatment. This, in essence, consists of the gradual saturation of the individual with scopolamine hydrobromide. This procedure is carried to the extent of producing delirium with its accompanying amnesia for the immediate past. The pharmacological action of scopolamine, both central (cortical) and on the peripheral nerve endings, motor, sensory and secretory, tends to combat the distressing withdrawal symptoms. After forty-eight hours pilocarpine is given, the direct antithesis of scopolamine in all respects save that of the cortical effect. In view of the induced hypocalcaemia, calcium is given during convalescence. The results of 57 cases so treated are very briefly discussed: 55 per cent were completely free of the habit when investigated three years after treatment; 12 per cent relapsed, and in 33 1/3 per cent no adequate data could be obtained.

The psychological factors are mentioned but hardly adequately stressed. In no case were there any unfortunate residual effects.

G. N. PATERSON-SMYTH

A Warning about Acidification Therapy in Cases of Renal Infection due to the Proteus Bacillus. Chute, R., *New Eng. J. M.*, 1936, 214: 869.

Indiscriminate acid therapy may lead to trouble. The proteus bacillus is a frequent invader of the urinary tract and produces an infection resistant to the ordinary methods of combating urinary infections. It rapidly splits the urea of the urine and produces ammonia, making the urine intensely alkaline. This alkaline infected urine greatly predisposes to the formation of calcium phosphate stones in the urinary tract. A case is described in which stones in the kidney were formed while the patient was under treatment for proteus bacilli infection. Acidification of the system greatly increases the excretion by the urine of both calcium and phosphorus. The rapid ammonia production by the proteus bacillus makes it difficult to keep the urine acid; therefore the phosphorus calcium was precipitated as stones in an alkaline urine.

The urine in infections of the urinary tract should always be cultured. What may be the proper régime in treating infections due to colon bacillus may be the wrong thing in dealing with infections due to the proteus bacillus. In cases of infections with the proteus bacillus ammonium chloride would seem to be unsuitable as a urinary acidifier for biochemical and bacteriological reasons. In treating infections of the kidneys with the proteus bacillus, systemic acidification may be dangerous and lead to the formation of new stones, unless one is successful in obtaining a strongly acid urine. This may be impossible due to the rapid manufacture of ammonia by the proteus bacillus.

LILLIAN A. CHASE

Pathology and Experimental Medicine

The Nature of the Peripheral Resistance in Arterial Hypertension, with Special Reference to the Vasomotor System. Prinzmetal, M. and Wilson, C., *J. Clin. Invest.*, 1936, 15: 63.

From the physiological point of view elevation of the blood pressure may be due to an increase in cardiac output, in the volume or viscosity of the blood, or in the resistance of the peripheral vessels. Since it has been shown by others that the cardiac output is not increased in hypertension and that the volume and viscosity of the blood are normal all that remains is increased resistance in the peripheral circulation. Investigation on this point has given conflicting results. The studies of the present authors were carried out on the blood flow in the arm under various conditions, using the arm plethysmograph described by Lewis and Grant. Determinations of resting blood flow in the arm in

various types of hypertension (benign, malignant, and secondary) gave an average value no greater than that obtained from subjects with normal blood pressure. This indicates that increased vascular resistance in the different types of hypertension is not confined to the splanchnic area but is generalized throughout the systemic circulation.

Persons with hypertension showed increase in blood flow in response to heat and reactive hyperæmia equal in degree to that produced in normal people, showing that the blood vessels in hypertension are capable of considerable dilatation and indicating that the increased peripheral resistance is due to hypertonus and not to organic changes in the vessel walls. Sympathetic vasodilatation produced by the "heat test" caused no greater increase in blood flow in persons with high blood pressure than in normal people, suggesting that the vascular hypertonus is not vasomotor in origin. Anæsthetization with novocain of the vasomotor nerves to the arm produced the same increase in flow in normal subjects and patients with hypertension, proving that the vascular hypertonus is independent of the vasomotor nerves, and that this hypertonus must therefore be regarded as the result of intrinsic spasm of the blood vessels themselves.

The above conclusions apply to all types of hypertension studied; namely, benign hypertension, malignant hypertension, and "renal" hypertension associated with acute and chronic glomerulonephritis and chronic pyelonephritis; hence there is no physiological evidence for the separation into "organic" and "functional" types, or for the assumption that renal hypertension is due to vasomotor hypertonus.

JOHN NICHOLLS

The Effect of Drugs in the Production of Agranulocytosis, with Particular Reference to Amidopyrine Hypersensitivity. Dameshek, W. and Colmes, A., *J. Clin. Invest.*, 1936, 15: 85.

Sufficient evidence has accumulated in the last two years to indicate the importance of various drugs as etiological agents in the development of agranulocytosis. Although multiple factors are probably at work in a given case it is apparent that the administration of a drug, usually amidopyrine, has frequently been the determining one. In twelve cases of agranulocytosis studied, although many factors seemed operating, the only constant one was a drug, usually amidopyrine, administered either alone or in combination. Of eight recovered patients four were selected for special study as regards possible hypersensitivity to drugs. The subjects were tested with amidopyrine, which was exhibited orally, by scratch test, patch test, intradermal test and passive transfer test. Finally, taking a hint from Horsfall, intradermal tests were performed with

a mixture of an aqueous solution of amidopyrine and blood serum. One patient reacted strikingly (within 90 minutes) to the oral administration of 0.6 g. (10 grains) of amidopyrine with the clinical and haematological manifestations of agranulocytosis. Two other patients developed moderate leucopenia and clinical reactions. The fourth patient, given 0.3 g. (5 grains) of the drug, developed no symptoms. The skin reactions to various scratch tests, patch tests, passive transfer tests, and intradermal tests with the drug and blood serum were strongly positive in three cases tried. Two of the three patients, shortly after the intradermal administration of amidopyrine solutions for skin testing, developed all of the clinical and haematological features of agranulocytosis. The total quantity of amidopyrine used in these tests did not exceed 10 mg. (one-sixth of a grain).

Numerous reports demonstrate that the use of drugs, particularly of amidopyrine, both alone and in combination, is an important cause of agranulocytosis. The widespread use of these drugs and the relatively few cases of this disease suggest idiosyncrasy or hypersensitivity on the part of certain persons. The author's results support this conclusion. The occurrence of agranulocytosis after the intradermal introduction of only a few milligrams of the drug tends to disprove the theory that the drug must be oxidized in the gastro-intestinal tract before it can become toxic. The negative intradermal tests when an aqueous solution of amidopyrine is used, as contrasted with the strongly positive results obtained with a "serumized" solution, suggests a possible drug-protein linkage as the basis of the "allergic" or hypersensitivity reaction.

JOHN NICHOLLS

Maternal Age at the Conception of the Congenitally Malformed Child. A Study Based on 607 Cases. Murphy, D. P., *Am. J. Dis. Child.*, 1936, 51: 1007.

The data in this paper were derived from 570 families in which were born 607 congenitally malformed children. The maternal age at the birth of the first normal and of the first defective child was ascertained. The interval from marriage to the birth of the first malformed infant was determined for two groups of mothers, those marrying at an average age of 16.8 years, and those marrying at an average age of 26.8 years. The ratio of defective to normal offspring at various maternal ages was determined. The conclusions arrived at are as follows. The average maternal age at birth of the first normal child was 23 years, while the average maternal age at birth of the first defective offspring was 28.4 years. When two groups of mothers whose average ages were separated by 10 years were studied it was found that the interval from marriage to birth was much longer

for the younger mothers than for the older, thus showing that the woman had to attain a certain age before she began to produce malformed children to any extent. The ratio of malformed to normal offspring increased as the maternal age rose. From these statistical conclusions Murphy arrives at the following sociological conclusions. Mothers should marry reasonably early if we desire to keep the number of congenitally malformed children at a minimum. They should have no more than four children, for it was noted that after the fourth child, the proportion of malformed children rose materially. They should give birth to their last child before 30 and as close to the age of 25 as possible.

Note.—It will be remembered that Still found the greatest number of malformed children to be the *first-born*, and promised immunity from malformations to children born after the first. In hereditary malformations, there has been shown to be no influence of maternal age on the appearance of the condition. The only way in which such results as Murphy's can be explained, if they are correct, is that they are the result of mutations which tend to occur more frequently in older ova. In the meantime it is going to be hard on the mother who has to crowd four children into a period of four to five years, unless we reduce the age at which girls are allowed to marry.

MADGE THURLOW MACLEIN

Hygiene and Public Health

Pulmonary Asbestosis: Incidence and Prognosis. Donnelly, J., *J. Indust. Hyg. & Toxicology*, 1936, 18: 222.

Donnelly reports the examination of 151 workers in asbestos mills: 52 of these showed definite evidence of asbestosis in varying stages. All except one had worked for more than 4 years. Of the advanced cases none had worked less than 8 years. Writers have differed somewhat as to the relationship of asbestosis to tuberculosis. Some consider that asbestosis tends definitely to exacerbate old tuberculous lesions, while others hold the contrary view. Donnelly's experience would appear to support the view that asbestosis does not activate tuberculous lesions. Only 4 of his cases (all of whom were skiagraphed) were diagnosed as probably active tuberculosis of the adult type. One of the 4 had worked only 5 months and the other 15 months in asbestos dust.

It is improbable that asbestosis could have been responsible for activating their lesions, particularly since the films in both cases indicated a chronic type of disease and not an acute exacerbation. The other 2 of the 4 had had 6 and 10 years' work in asbestos, respectively. Two cases in 151 can hardly be considered more than a normal incidence. One case of old tuberculosis was followed by x-ray over a period of 5 years. Although this man apparently developed asbestosis his tuberculous lesion remained inactive.

Probably the most frequent terminal result in asbestosis is progressive cardiac failure.

FRANK G. PEDLEY

A Survey of a Group of Employees Exposed to Asbestos Dust. McPheeters, S. B., *J. Indust. Hyg. & Toxicology*, 1936, 18: 229.

This paper reports the results of a survey of 210 persons exposed to asbestos dust. A clinical examination was made and a flat x-ray plate taken on each. Thirty-three cases of definite asbestosis were diagnosed; 31 of these cases had been exposed for more than 5 years; 2 between 2 and 5 years. No activating or aggravating effect of asbestos dust or asbestosis on tuberculosis was observed.

FRANK G. PEDLEY

Urology

A Skin Test for Diagnosis of Gonococcus Infections. Corbus, B. C., *J. Urol.*, 1936, 34: 112.

The author introduces the gonococcus bouillon filtrate (Corbus-Ferry) as a diagnostic and therapeutic substance in the treatment of gonococcal infections. The filtrate he specifies contains two specific substances. The one when injected intradermally is probably taken up by the histiocytes of the skin, and produces a gonococcal antitoxin. The other presumably combines with sensitizing antibodies and produces a typical allergic response in those infected with the gonococcus. The cutaneous reactions are read on this basis, the large inflammatory zone being the antitoxin-forming area, and the central zone of darker red hue, the sensitizing response. The author believes he has been able to eliminate the false positive reactions by removing the first specific substance by autoclaving and thereby obtaining a reading of the allergic factor. The author feels that gonococcal infections for the most part are not difficult to diagnose clinically. However there exists a large group of cases comprising mostly women, children, arthritics, and patients with chronically infected prostates, where this is difficult to accomplish. The test is based entirely on the allergic state of these individuals, and since this allergic state ceases with the disappearance of the gonococci it may help to clarify many previously mistaken diagnoses and in addition furnish a specific test for a clinical cure.

V. J. BERRY

The Bactericidal Effect of Levorotatory and Racemic Beta-oxybutyric Acid in Urine. Helmholtz, H. and Osterberg, A. E., *J. Urol.*, 1936, 34: 86.

The writer discusses the bactericidal action of ketonuria and only recently discovered that such action was due to the levorotatory beta-oxybutyric acid. In a series of experiments

using the common groups of organisms infecting the urinary tract, he finds that urine containing 0.5 per cent beta-oxybutyric acid at a pH of 5 constantly had bactericidal action on these organisms, and that there is an increasing bactericidal action when there is an increase in the concentration of beta-oxybutyric acid from 0.5 to 2.5 per cent. When a patient is in ketosis beta-oxybutyric acid taken by the mouth appears in large measure in the urine, so that by feeding of the racemic acid the concentration for bacteriostasis can be obtained. He concludes from the experiments that the action of the racemic acid was strikingly similar to that obtained with the levorotatory acid.

V. J. BERRY

Retention of Urine in the Fetus. Bynnm, T., Jr. and Cooper, S., *J. Urol.*, 1936, 34: 93.

The authors present the case of a premature male child which had been a very difficult birth problem because of a very markedly dilated urinary bladder. The child voided subsequently to birth but died on the 6th day in coma. It was interesting that apart from a few red blood cells the urine was normal. Autopsy revealed a normal urethra and a markedly dilated bladder. The left ureter presented strictures at 1.5 and 7 cm. above the bladder, and bilateral hydro-ureter. The renal pelvises were greatly dilated, with obliteration of the calyces. The right kidney was small and atrophic and showed considerable interstitial fibrosis.

The authors report two similar cases from the literature, causing dystocia of labour, which they attribute to idiopathic atony of the bladder. This case would also seem to substantiate the opinion already accepted that the fetal kidneys secrete urine and that urine is passed *in utero*. It also demonstrates how rapidly back pressure can cause destructive urinary tract lesions in these young children.

V. J. BERRY

Outside this place of suffering and tears,
A city sleeps in silence undismayed,
Unknowing of the thousand lashing fears,
By which the hours of dark are coldly flayed;
The night lights gleam; the busy streets are still;
No sign of life or movement is revealed
Where winter frost in beauty claims the hill,
And distant shadows pattern snowy field.

Within this place the tide of life sweeps on:
From birth to death, through tragic interlude,
There is no rest; and footsteps till the dawn,
Will beat upon my brain in tumult rude.
The quarter hour: Dear God! If I could sleep,
I might forget how slowly minutes creep

—Clara Bernhardt, Maplegate, Preston, Ont.

Obituaries

Dr. Frank Manson Brown, of Centreville, N.B., died at the Fisher Memorial Hospital at Woodstock on June 21, 1936, at the age of 72 years. He had been ill for a considerable period. Dr. Brown was born in Douglas, graduated in medicine from Columbia University (1885), and had done post-graduate work in Edinburgh. He is survived by his wife, one daughter, and three sons.

Dr. Graham Chambers, of Toronto, died on March 27, 1936, after a lingering illness. Dr. Chambers was in his seventieth year and a member of the staff of the University of Toronto.

Born in Woodstock, Dr. Chambers was educated at the public and high schools of the town and graduated from the University of Toronto in medicine in 1889. He established himself in Toronto, specializing in skin, stomach, and x-ray work. As professor of Internal Medicine, he was on the staff of the Toronto General Hospital for many years. He was an emeritus professor of Chemistry in the Ontario College of Pharmacy.

With the outbreak of war, Dr. Chambers enlisted with the University of Toronto Hospital, which was sent to Saloniki. At the close of the war he was returned to Orpington, Kent, and later joined the staff of Moore Barracks, Shorncliffe, England. He retired with the rank of Lieutenant-Colonel.

Following his return from overseas service, Dr. Chambers's health declined, and in 1921 he went to Northern Ontario to regain it. While tramping through the woods at a spot near Atikokan, northeast of Fort Frances, he became lost. For two weeks he was the object of an intense search, and, when found by three searchers, it was learned that he had lived on berries and nuts. Aeroplanes were used in the search for him.

For the last fifteen years Dr. Chambers had not practised actively in Toronto.

He is survived by his widow, formerly May Rogers.

Dr. Ernest Gariepy, a member of the Faculty of Medicine, University of Montreal, died about May 26, 1936. He was born in 1879 and was a graduate of Laval University, Montreal (1916). He is survived by a son and two brothers.

Dr. Robert Michael Hillary, of Aurora, Ont., died June 1, 1936. Dr. Hillary was the eldest son of the late Dr. Robert W. Hillary, of Aurora, and a graduate of Trinity Medical College (1890). He is survived by his widow, Edith Howard Mussen.

Dr. Joseph Omer Pichette, aged 65, was found dead in his office in Montreal on June 26, 1936. From indications, he had been dead some days.

Born in Joliette, Dr. Pichette received his early education there and then came to Montreal to study medicine at Laval University. Following his graduation (M.D., 1893), he practised for 12 years in Ligouri, Que., and then returned to Montreal, where he practised up to a short time ago, when he retired. Besides his wife, he is survived by six sisters.

A GOOD DEED.—Each ray of light from a distant star has been travelling on through the ether for hundreds of years. Yet it still remains pure and strong enough to affect the negative plate of the astronomer's camera. So with a good deed—set it going, and who knows the end of it? Not the world of this century or the next, for its influence will travel on for ages to come.

News Items

Great Britain

The Birthday Honours.—The first list of honours to be conferred by King Edward VIII was issued on Tuesday, June 23rd, and the item with which it opens will be welcomed by the whole medical profession. Lord Dawson of Penn's personal services to King George V throughout his reign, and in a special degree during its last eight years, are fittingly acknowledged by the conferment of a Viscounty—the first time this honour has been given to a practising medical man. During his long connection with the London Hospital Lord Dawson went through all the ranks of a large medical school, and he has been dean of the medical faculty of the University of London. In the war of 1914-18 he was consulting physician with the British Armies in France; he is now, for the sixth year in succession, President of the Royal College of Physicians of London; and he was President of the British Medical Association on the occasion of its centenary celebrations in 1932. As Physician-in-Ordinary to King George he bore by far the heaviest part of the responsibility of the long and grave illness in the winter of 1928-29, and of the last illness five months ago. In all the high posts held by him Lord Dawson has proved himself thoroughly sympathetic with the forward movement in medical science, practice, and organization. It is not too much to say that Lord Dawson's wisdom at the bedside and in council is regarded as a national possession.

Long and valuable service to the Throne is recognized also in the promotion to Knight Grand Cross of the Royal Victorian Order of Sir Richard Cruise, surgeon-oculist to the King. Dr. Arthur MacNalty, who became Chief Medical Officer to the Ministry of Health and the Board of Education last year, is created Knight Commander of the Bath; and so is Surgeon Vice-Admiral Robert Hall, Medical Director-General of the Royal Navy since 1934.

Alberta

There is an increasing tendency for municipalities to offer some type of contract to medical men in Alberta, otherwise they will have no one to care for their sick. Recently the Barons district made a contract with the local physician who enters on a complete medical contract wherein he renders services to the full of his ability for a definite annual salary.

The Council of the College of Physicians and Surgeons recently ordered the erasure of the name of an Alberta practitioner for dispensing narcotic drugs for other than medicinal purposes. Owing to the fact that the physician had been heavily fined, and, further, was in a pioneer district where remuneration was small, the sentence was suspended during good behaviour.

At the last session of the Alberta Legislature a Bill was passed, to collect a special tax which would create a fund for the care of tuberculous patients. Arrangements have been made by which certain portions of three hospitals in Edmonton, viz., the Royal Alexandra, University, and the General Hospitals are available for patients; these in addition to the Central Alberta Sanatorium, Calgary. All applications must be made to the Sanatorium, and the beds are thus allocated having regard to residence and vacancies. The province does not collect from the patient, but covers the expense of the care and treatment from the fund.

The Annual Meeting of the Canadian Medical Association, Alberta Division, will be held in Calgary, Palliser Hotel, September 15, 16 and 17, 1936, the first day being taken up with business and various matters affecting the profession generally. The second

and third days will be for scientific papers. A time will be set apart for the Annual Meeting of the College of Physicians and Surgeons, when all registrants will be expected to bring forward any questions they consider of sufficient interest. Three outside speakers are expected to be present and contribute to the program, the balance being taken by local men of the province.

Three Annual Meetings of the District Societies will be held the latter part of July, *viz.*, Drumheller, July 28th, Red Deer-Stettler at Red Deer, July 29th, and District No. 4 at Camrose, July 30th, next.

Dr. A. J. Fisher, President of the Calgary Medical Society, has just left for a post-graduate course in New York City, expecting to return in November.

G. E. LEARMONTH

British Columbia

The Vancouver City Council has been pressing the Provincial Government to establish the headquarters of the Health Insurance Commission in Vancouver, but the Government has announced that the offices will be in Victoria, although a subsidiary office may later be opened in Vancouver.

An international health convention, at which representative public health officials from Canada, United States, Alaska and Hawaii were present, was held in Vancouver under the chairmanship of Dr. J. W. McIntosh, the medical officer of health for Vancouver, on June 22nd. "Health Week" of which the convention was the central feature was thus inaugurated by the Greater Vancouver Health League. The organizations taking a leading part were the Canadian Tuberculosis Association, the American Public Health Association, the State and Provincial Health Authorities of North America, and the British Columbia Public Health Association. There was an attendance of about 600.

Noteworthy figures in the monthly bulletin of the Provincial Health Department for May were 2,975 cases of measles, 114 of tuberculosis and 91 of cancer; 79 deaths out of a total of 630 in April were due to cancer. It is understood that the cancer cases were reported from institutions, practically none being reported by private practitioners.

In view of the published estimate by Dr. W. H. Walsh, of Chicago, who recently made a survey of the Vancouver General Hospital, that health insurance would mean an increased demand for hospitalization of 15 to 20 per cent, the Associated Property Owners of Vancouver have urged the municipalities to take precautions that such extensions as may be necessary from this cause be not wholly charged to the City. The Council have drawn this matter to the attention of the Hon. G. M. Weir, the provincial secretary.

D. E. H. CLEVELAND

Manitoba

At the request of the United Farmers of Manitoba the College of Physicians and Surgeons sent several doctors to attend Chataqua meetings held by the United Farmers and to give an address on the theme, "What to do until the Doctor Comes".

At the annual meeting of the American Dermatological Association, held at New Ocean House, Swampscott, Mass., on June 4 to 6, 1936, Dr. A. M. Davidson was elected a member of the Association. He is the third active Canadian member.

In response to a questionnaire sent to rural practitioners in Manitoba by the Committee on post-graduate studies there was an almost unanimous request for a course in obstetrics and gynaecology. Such a course is

now being prepared by the committee for the annual post-graduate course which will take place during the next college year.

ROSS MITCHELL

New Brunswick

The quarterly meeting of the Association of Officers of Medical Services of Canada, New Brunswick Branch, was held in connection with the Officers' Mess, 14th Field Ambulance, at Sussex Camp during militia training. An exceptionally large number were present and were entertained by the officers of the Ambulance in command of Lt.-Col. V. D. Davidson, V.D. This organization is in a flourishing state and interest in its activities has been well maintained.

The medical profession in New Brunswick were shocked to hear of the death of Mrs. Murray MacLaren, wife of the Hon. Murray MacLaren, M.D., Lieutenant-Governor of the Province. Mrs. MacLaren had always held a very warm place in the hearts of her husband's medical colleagues. Her death occurred in Saint John on July 12th immediately on her return from a trip to Europe.

A. STANLEY KIRKLAND

Nova Scotia

Ways and means of raising money and health insurance were the outstanding topics under consideration at the annual meeting of the Hospital Association of Nova Scotia and Prince Edward Island, held at Truro, on July 8th and 9th. The Honorary President, Rev. H. G. Wright, of Inverness, in his paper, "The problem of the indigent patient", introduced an appeal for a central fund made up by the Provincial Government and contributions of citizens. Such a fund, he hoped, might save the small hospital from being engulfed by its ever-mounting uncollected accounts. Mr. Wright felt that the problem was not one for the government alone; it had grown too great for the municipalities; hence, his plan. Dr. Dunbar felt that the prevention of indigency would furnish a more elemental solution.

Health insurance was taken up by Dr. A. H. Agnew, and his excellent paper elicited much discussion. The hospital system of the Nova Scotia mining areas was presented as an ideal one for its purpose, an example which might be followed by other industries.

The matter of free postage for x-ray films, so that small hospitals without attending roentgenologists (especially tuberculosis annexes) might more readily get expert advice, was referred to the Canadian Hospital Council.

The necessity of clear and concise hospital records was stressed in an address by Dr. T. P. Ponton, of the American College of Surgeons.

All the officers of the past year were re-elected: *Honorary Presidents*, Rev. H. G. Wright, Inverness, W. R. Rogers, Charlottetown. *President*, Dr. D. J. Hartigan, New Waterford. *Vice-presidents*, A. J. MacDonald, Glace Bay, Rev. Sister Anna Seton, Halifax. *Secretary-Treasurer*, Miss Anne Slattery, Windsor. Next year's meeting will be held at Sydney.

Only three school children of the 13,540 on the Halifax School registers died during the past year, according to statistics of the School Commission. This is believed to be an all-time record for good health among the young people of the city.

Dr. Alexander MacDonald, son of Dr. Dan MacDonald, has taken over the North Sydney practice of Dr. C. O. Walsh.

In the world of sport, Dr. C. S. Henderson became president of the Parrsboro Golf Club, and Dr. F. R. Shankel President of the Windsor Tennis Club.

The sale of codeine in Nova Scotia is not excessive, and there is no evidence of its abuse within the province,

members of the Nova Scotia Pharmaceutical Society agreed. They were in annual convention at Windsor.

Dr. James A. Muir (Dal. '36) has taken over the practice of Dr. J. Sinclair Robertson, of Mulgrave. Dr. Robertson was recently appointed health inspector for Cape Breton Island. His headquarters will be Sydney.

Dr. H. E. Kendall, Curry's Corner, sailed recently on the *Empress of Britain* as a Nova Scotian delegate to the Empire Fruit Conference in London.

Dr. L. R. Meech has been appointed coroner to the town of North Sydney.

"Old Graduate", an anonymous donor of ten thousand dollars to Dalhousie University some years ago, has been revealed as Dr. J. A. Lippincott, Dalhousie's oldest living graduate. In 1867 Dr. Lippincott took his Arts degree from Dalhousie, graduating later from the Jefferson Medical School. Recently Dr. Lippincott returned to renew old Dalhousie acquaintances. Until his retirement, only a short time ago, he was practising his specialty, diseases of the eye, in southern France. He was born in New Glasgow in 1847.

Delegates to the convention of United Mine Workers at Glace Bay were definitely opposed to any reduction in the medical check-off and the services rendered by the doctors was highly lauded. They declared that the physicians were far from being overpaid, and that they were giving a service, which, from the financial standpoint, could not be duplicated elsewhere in Canada.

ARTHUR L. MURPHY

Ontario

On Tuesday, June 9th, the Hastings and Prince Edward Medical Society, with representative citizens, gave a complimentary banquet to Dr. W. M. Mather, of Tweed, on the occasion of his completing fifty years of service as a medical practitioner in Hungerford Township. A gold-headed cane was presented to Dr. Mather by the Hon. Doctor Faulkner on behalf of his fellow practitioners and friends.

With the merging of Grace Hospital and the Toronto Western Hospital the Board of Governors announced important changes in the medical staff, effective July 1st. Dr. T. A. J. Duff has been appointed surgeon-in-chief, succeeding Dr. H. E. Clutterbuck, who is retiring; Dr. H. K. Detweiler succeeds Dr. F. A. Clarkson as Chief of the Medical Division.

The address given by His Honour, the Lieutenant-Governor of Ontario, Dr. H. A. Bruce, at a recent conference on social welfare in Toronto on the subject of sterilization and the problem of the mentally unfit, appears in *MacLean's Magazine* for July 1st.

General Order No. 18 authorizes the formation of a Canadian Army Medical Corps Rifle Association, with headquarters at Toronto.

The appointment of Maj.-Gen. J. T. Fotheringham, C.M.G., V.D., Retd. list, as Honorary Colonel of the Royal Canadian Army Medical Corps is extended to March 15, 1941.

Major F. R. Hassard, M.C., Major W. G. Cosbie, M.C. and Major T. H. D. Storms, V.D., have been promoted Lieutenant-Colonels in the C.A.M.C.

J. H. ELLIOTT

Saskatchewan

Drs. D. M. Baltzan and H. E. Alexander, of Saskatoon, gave a very thorough symposium on the thyroid, from the medical and surgical aspects, at the May meeting of the Prince Albert Medical Society.

While Dr. C. W. Thorne, of Melfort, is taking post-graduate work in England, Dr. D. Sutherland is looking after his practice.

Dr. J. Ganshorn has joined Dr. M. I. Humphries and Dr. G. H. Lee in their practice in Prince Albert.

Dr. C. H. Andrews, of the staff of the Prince Albert Sanatorium, is taking post-graduate studies in Philadelphia.

For the June meeting of the Prince Albert Medical Society, Dr. U. J. Gareau and Dr. H. C. George of Regina made an aeroplane visit to Prince Albert. Dr. Gareau addressed the meeting on "Internal hæmorrhage in the new-born"; Dr. H. C. George, on "Heart disease, angina pectoris, coronary thrombosis and effort syndrome".

Dr. D. P. Miller attended the Canadian Medical Association meeting at Victoria, and Dr. B. W. Kirkby gave an address at the Canadian Tuberculosis Association in Vancouver.

LILLIAN A. CHASE

United States

American Congress of Physical Therapy.—Announcement is made of the 15th annual clinical and scientific session of the American Congress of Physical Therapy, September 7th, 8th, 9th, 10th and 11th, at the Waldorf-Astoria, New York City. The program includes many special features; sectional meetings in the specialties, symposia on short wave diathermy, hydrotherapy, exercise and electro-resection. Fever therapy and the treatment of vascular diseases occupy an important place and will be discussed by prominent workers in the field. The educational aspects of physical therapy and the relationship of physical therapy technicians to physicians and hospital departments will be thoroughly dealt with. Other features include technical and scientific exhibits and a full day of hospital clinics where technique will be adequately demonstrated.

Physicians, their technical assistants, and nurses working in institutional departments of physical therapy are urged to attend this important session. There will be no registration fee.

A Cash Award of \$1,000 is offered by the Williams and Wilkins Company for the best manuscript on a science subject presented before July 1, 1937. Literary prizes are relatively common, but it is not so usual for a publisher to be bidding for science material in this manner. The publishers put no limitations on the subject-matter or manner of handling, and none on eligibility for the award. The MS. must be in English and "of a sort calculated to appeal to the taste of the public at large". The desired length is given as 100,000 words. While any MS. on a science subject will be considered, it is expected that the author will prove to be a man or woman engaged in a scientific pursuit, and who is possessed of the requisite literary skill to interpret science for that portion of the public which reads books. To assure authenticity, the publishers have enlisted the services of some 25 or 30 "advisers", these being men of science of wide reputation and assured competence. One or more of the advisers will pass upon each MS. from the viewpoint of soundness and accuracy. The award will lie in the joint discretion of four judges selected with a view

to their especial qualification in choosing the sort of book that will appeal.

The judges are Dr. Joseph Wheeler, Librarian of the Pratt Library, Baltimore, and chairman of the Book List Committee of the Association for the Advancement of Science; Harry Hansen, reviewer and critic for the *New York World Telegram* and *Harper's Magazine*; Dr. Lyman Bryson, Professor of Education of Teachers' College Columbia, and Director of the "Readability Laboratory"; and David Dietz, science editor of the Scripps-Howard newspapers.

Further details concerning the award may be had by addressing the publishers at Mt. Royal and Guilford Avenues, Baltimore, Maryland.

The honorary degree of Doctor of Science has been conferred upon Dr. Lawrason Brown, Consulting Physician, Trudeau Sanatorium, Saranac Lake, by the Medical College of Virginia, on the occasion of the commencement exercises closing the 98th session of the College on June 2nd.

General

The First International Congress of Sanatoria and Private Nursing Homes will be held from September 16th to 21st, in the rooms of the Academy of Sciences, Budapest, Hungary. Communications should be addressed to Prof. Dr. Benczar, Szt. Margitsziget Szanatorium, Budapest.

Book Reviews

The Early Diagnosis of Malignant Disease. Malcolm Donaldson, F.R.C.S., M.B., B.Ch., F.C.O.G., and others. 168 pages. Price \$2.75. Oxford University Press, London; McAllinsh & Co., Toronto, 1936.

The preface to this excellent little book significantly states that, while some 56,000 people die of cancer in one year in the British Isles, there are over 57,000 medical men and women to care for the patients. It follows that few physicians have any extensive experience in recognizing the early manifestations of cancer. The five authors have among them dealt with twelve systems or areas of the body in which cancer may be diagnosed, and have indicated the symptoms which arouse a suspicion of the disease and the signs by which it may be recognized. It is admitted that early diagnosis of new growths in the upper air passages, oesophagus, lung or mediastinum may be very difficult. "A patient with hay fever is much more apt to consult his doctor than is one suffering from cancer." Certain neoplasms in the gastro-intestinal tract may cause very little disturbance until they have developed to a dangerous stage, but as a rule signs are present and may be recognized by the doctor who is "cancer conscious".

Very little space is given to treatment, but the point is made that when radiation is to be used an adequate dose be given at once. The gospel of a second chance does not apply to radiation therapy.

The reviewer feels that the compression of material has been overdone, but at the same time hopes that the book may have a wide circulation, as its content is really worth while.

Clinical Miscellany. The Mary Imogene Bassett Hospital, Cooperstown, N.Y. Vol. 2, 218 pages, illustrated. Price \$3.00. Charles C. Thomas, Springfield, and Baltimore, 1935.

The profession will welcome the second volume of a potentially indefinite series of perfectly recorded case-reports of unusually interesting clinical material. In the January, 1935, number of this *Journal* the first volume was reviewed and favourable comment was made

upon the underlying idea of placing on permanent record a number of cases that will serve as important references for all time. It was pointed out that medicine might well take the example of law in establishing "precedents" for the guidance of its practitioners. There is no doubt that in reading up a disease one is able to get a more concrete visualization of it from well reported cases than from a number of glittering generalities such as constitute the average textbook description. This dictum is not meant as a depreciation of the latter by any means, but is designed to emphasize the importance of necessary illustrations in the form of actual *bona fide* cases. In our previous review it was stated that Volume 2 would be welcome when it came. This was no false prophecy. Much that was said in praise of Volume 1 applies to Volume 2. Indeed Volume 3 will be equally welcome when it comes, and if the same standard of excellence continues to be maintained a valuable series may be eventually established as permanent *res gratie* among discriminating library builders. It is suggested that an identical type of attractive volume may be perpetuated for uniformity in the book-shelf.

Human Pathology. Howard T. Karsner, M.D., Professor of Pathology, Western Reserve University. Fourth edition, 1013 pages, illustrated. Price \$11.00. J. B. Lippincott, Philadelphia, London and Montreal, 1935.

A new edition of a standard text such as this calls for no great comment from the reviewer. This work has run to four revisions in ten years and therefore has kept up to date. The subject matter includes the usual material found in textbooks on pathology, treated in an efficient manner. The book suffers from the effort to encompass the vast field of general and special pathology in a little less than a thousand pages, with a resultant cramping of material and jerky style. However, it has been a favourite throughout its three previous editions, and with the general revision there is little that is not covered. The illustrations are becoming better with each edition, many of the newer ones being excellent, but in common with many another text in pathology the illustrations portraying inflammation, the degenerations, and disturbances of circulation do not give a real picture of what is seen through the microscope, nor are they diagrammatic enough to give information in that way. The student striving to visualize a process is, as often as not, confused by this type of illustration. The newer photographs of specimens are, on the other hand, commendable and most valuable.

Students will probably read the text recommended by their particular professor rather than by this reviewer, but, the latter has no hesitation in recommending this book as an authoritative and complete text to any graduate who may wish an up-to-date reference in pathology.

An Introduction to Public Health. Harry S. Mustard, M.D., Associate Professor, Public Health Administration, Johns Hopkins University. 250 pages. Price \$2.50. Macmillan, New York and Toronto, 1935.

As an introduction to Public Health this book is by far the best that has appeared. Those who know Doctor Mustard will not be surprised at its soundness. Those who have read his previous publications are already familiar with his lucid and succinct smoothness of expression. Here is a satisfactory textbook for undergraduate medical students and others who require a reliable text which will guide them to a sound philosophy of the subject. It also furnishes the basic information, and is a keen, stimulating and pungent analysis of trends and of public health practices. The book will be read with interest and pleasure by all public health workers and medical practitioners.

Doctor Mustard considers that "public health work, including medical care, is but one of many social measures". His remarks on the provision of medical

care are particularly timely. "If systematized public action is necessary for providing medical service, then ordinary sickness becomes a public health problem". "... the problem of providing high-grade medical service at low cost has become a sociological one, and may, in part, be transferred to health departments, representing government."

The book fits into the teaching of those who have a social viewpoint and who consider that the medical practitioner should be a practitioner of preventive medicine; what he has learned in public health does not make him an amateur sanitary engineer, but renders him competent, as a practitioner of preventive medicine, to participate in public health as related to the whole public health program.

Doctor Mustard is to be congratulated upon an altogether admirable piece of work. He has accomplished the difficult task of writing an introduction to the subject without becoming involved in details and yet not omitting the essentials. This book is recommended without reservation to students of public health.

An Introduction to General Therapeutics. H. K. Fry, D.S.O., M.D., B.Sc., D.P.H., Lecturer in Materin Medica and Therapeutics, University of Adelaide. 223 pages. Price \$1.75. Cassell & Co., London; McAinsh & Co., Toronto, 1935.

In the preface to this octavo volume the author somewhat disarms the reviewer by admitting the rashness of trying to put a subject so large in a compass so small. Thus we are not unprepared for the sketchy fashion in which some of our important remedies are treated. At the same time it may be said fairly that the space is not always allotted to the best advantage and that there is a disproportion in the emphasis placed on the various therapeutic remedies enumerated. Digitalis and quinidine are drugs which are frequently prescribed, and their action is still a matter of discussion or dispute, but in this book they receive only a passing notice. On the other hand, the physical properties of the x-ray and radium are given, although, in this country at least, the prevailing view is that radiation therapy is a specialty and not to be casually employed by the practitioner who has not had adequate training in its use. Nevertheless, the book has real merit and its appearance is timely. We are now emerging from an era of therapeutic nihilism, and a sober statement of what is valuable in the armamentarium of the physician is necessary—diagnosis alone is not enough if patients are to be satisfied with what the regular physician has to offer. Prof. Fry's pronouncements are remarkably sane and in accord with the experience of informed physicians, even if enthusiastic representatives from our drug houses may find them a trifle dampening. The book can be recommended for medical students, and it is also a safe guide for the general practitioner who is trying to find his way in the storm of remedial measures from press and radio by which he and his patients are now assailed.

Treatment in General Practice. Articles republished from the *British Medical Journal*. 248 pages. Price 8s. 6d. net. H. K. Lewis, London, 1936.

This is the first of a series of volumes in which are reproduced articles on treatment published from time to time in the *British Medical Journal*. The guiding principle has been to make these articles practical, above all things, and to keep them short and to be easily consulted. The principle has been strictly adhered to and the result is just what has been aimed at, i.e., articles on the treatment of the major medical disorders, written clearly and concisely. Just as important as this, however, is the fact that the contributors themselves are all well known men of wide experience and tested judgment. We have nothing but praise for this compact and valuable set of articles, and await with interest further volumes along the same lines.

Textbook of Pathology. Delafield and Prudden. Sixteenth edition, edited by F. C. Wood, Director of Pathological Department, St. Luke's Hospital, New York. 1406 pages, illustrated. Price \$10.00. Wm. Wood, Baltimore, 1936.

The editor of this work, Dr. F. C. Wood, tells us that in this edition the book celebrates a kind of jubilee, the first edition having been printed in 1885. Not many books continue to be so successful after the original authors' decease. It is evidence not only of solid foundations but of wise and expert editing that it has retained its popularity and maintained its original high standard.

Synopsis of Clinical Laboratory Methods. W. E. Bray, B.A., M.D., Professor of Clinical Pathology, University of Virginia. 324 pages, illustrated. Price \$4.25. C. V. Mosby, St. Louis; McAinsh, Toronto, 1936.

This is a rather unusually elaborate synopsis of clinical laboratory methods. The illustrations are profuse; several are in colour; and the text is comprehensive and well prepared.

Glandular Physiology and Therapy. A Symposium prepared under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association. 538 pages. Price \$2.50. American Medical Association, Chicago, 1935.

This is a symposium of papers on glandular therapy prepared under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association. It is pointed out in the introduction that some years ago the Council prepared a somewhat similar series of articles on the subject, having in mind the evident abuse of preparations of glandular materials, and there was no doubt of the value of that effort to clarify the knowledge that we possessed then. Since that time, however, there has been an immense accretion of work on the glands of internal secretion, and it is timely that this work should again be summarized for the profession. This has been done by a long series of investigators whose names are all well known in this work. They have produced an exceedingly useful collection of authoritative writings on this widely discussed and important subject.

Social Security. E. H. Ochsner, B.S., M.D., F.A.C.S., Consulting Surgeon, Augustana Hospital, Chicago. 281 pages. Price \$0.50. Social Security Press, Chicago, 1936.

As a young physician, Doctor Ochsner assisted at a German Krankenkasse and at similar institutions in Austria and Sweden. He was for four years president of the Illinois State Charity Commission. He is now retired from active practice and writes: "As one who loves his profession, I protest most vigorously against the mechanizing and mediocritizing of the medical profession; as a taxpayer, I object to adding to our already burdensome taxes; and as an American citizen, I am opposed to the breaking-down of the morale of my fellow-countrymen, which, I believe, is the inevitable consequence of any system of Social Insurance which could be devised." It is noted that the author does not include Workmen's Compensation as one of the social insurances.

In the opening chapter, the author complains against laws in general. He thinks it unfair that the crook can secure all the fire-arms he wants by mail-order while "the respectable law-abiding citizen finds it practically impossible to adequately protect himself and his property".

Various writers have presented their views on who won the war. It is refreshing, to say the least, to read that "Social Insurance may have actually prolonged the World War".

Doctor Ochsner's objection to all social insurance is set forth in a series of chapters. He considers social insurance undemocratic because it will "undermine

of the work. An example is the treatment outlined for appendicitis. A casual reader would have difficulty in appreciating the honest difference of opinion which exists regarding the best way in which to deal with appendicitis. Amongst so much which is excellent it may seem invidious to differ from the author. The extraordinarily rapid recovery after nerve suture recorded on page 609 must surely be based on a mistaken observation.

Altogether an excellent and concise text.

Meyer's Normal Histology and Histogenesis of the Human Teeth and Associated Parts. Translated and edited by H. R. Churchill, School of Dentistry, University of Pennsylvania. 305 pages, illustrated. Price \$5.00. J. B. Lippincott, Philadelphia, London and Montreal, 1935.

This text-book deals almost exclusively with human dental histology and histogenesis. The first half of the book gives a detailed description of the histology of teeth in their mature state, while the second gives a complete account of the process of histogenesis as observed in those teeth which eventually will be shed and also in those which will be permanent. Of the latter, the twenty which succeed the deciduous teeth have been named the "successional" teeth. There are 26 photomicrographs in colour which give a very realistic reproduction of the appearance of sections after staining with hæmatoxylin and eosin. A feature of the chapters on histogenesis is the inclusion of several series of drawings of serial sections which illustrate the stages of development as described in the text. Numerous photographs of models of developing teeth and surrounding parts also greatly facilitate the interpretation of the text. The second chapter from the last presents diagrammatically and also as seen *in situ* the relations of the deciduous and permanent teeth at various ages. The final chapter gives a tabulated review of tooth development from 7 weeks to 18 years.

In describing the dentin the possibility of nerves being present in the dentinal tubules is discussed. The author seems to accept the available evidence as positive, while the translator feels that there is need of further proof. In a critical examination of this book it may be noted that there is nothing in the first pages to indicate the author's standing among dental scientists. In several instances the phraseology in the text is so arranged that it does not readily convey the author's meaning to the reader. There is a tendency to employ words which are not in common use in works on dental histology. The proofreaders have overlooked the incorrect use of the double symbol ($\mu\mu$) when indicating microns (μ).

An Enquiry into Prognosis in the Neuroses. T. A. Ross, M.D., F.R.C.P. 194 pages. Price \$3.00. University Press, Cambridge. Macmillan Co., Toronto, 1936.

This is a book which may be recommended without reservation to every person who is interested in mental illness. Its lucid exposition of the cause, treatment, and prognosis in some of the less malignant forms of mental disorder should appeal not merely to the specialist in psychiatry but also to anyone who is concerned with advances in mental hygiene. The material is of particular interest to the practising psychiatrist inasmuch as the author has had an opportunity to follow the progress of a large group of neurotic patients for several years after discharge from hospital.

The author denies any claim to have written a treatise on treatment. None the less, the opening chapters will be found to contain some valuable remarks on therapy. The kinds of psycho-therapy in use at the Cassel Hospital (where the studies for this book were made) have been hypnotism, persuasion and analysis, with little emphasis on the first. It ap-

pears that Dr. Ross has paid little heed to the dicta of the Freudian school, and that his use of persuasion and analysis is of a kind not unfamiliar on this continent. Particular mention may be made of the chapters which deal with the outcome in certain groups of neuroses; as the author says, "Every kind of neurosis does not carry the same risk". The highly favourable prognosis in some kinds of neuroses, such as *anorexia nervosa*, should be of particular interest to the practitioner who has to deal with an occasional patient suffering from this type of illness.

A Study of Masturbation and the Psychosexual Life. John F. W. Meagher, M.D., F.A.C.P. Third edition, re-edited and revised by S. E. Jelliffe, M.D., Ph.D., 141 pages. Price \$2.00. Wm. Wood & Co., Baltimore, 1936.

The author is frankly a follower of Freud, and he refers to Rank, Jung and others as those who "for purely personal reasons have sought to establish divergent schools of their own". The first half of the book is given over to consideration of the development of the individual which provides the background for the chapters on masturbation. The author concludes that infantile masturbation is practically universal and common in adolescents. The practice is physiological in very young children, but is deleterious in adults, as it shows a psychosexual maldevelopment. The harm from excessive indulgence lies chiefly in the mental and moral spheres. Sympathy and encouragement are great aids to the patient. The best treatment is enlightened psychotherapy, the results of which are best where the traits and trends of the adolescent or adult are good and the wish to give up the habit strong.

Convalescent Care in Great Britain. Elizabeth G. Gardiner, Assistant Professor and Supervisor of Medical Social Work, University of Minnesota, 163 pages. Price \$1.50. University of Chicago Press, Chicago, 1936.

Convalescent care has not received in Canada the consideration which the subject warrants nor the consideration which has been given to it in Great Britain. A very extensive system of convalescent hospitals has been developed in the British Isles, and these institutions have proved an extremely valuable adjunct to the treatment given in the hospitals for acute diseases. Some of the institutions have been developed to a very high degree of efficiency. In this study Professor Gardiner has made a very interesting survey of the work done in Great Britain, and her book contains much information of value to the student of this subject. However, it is a factual review rather than a guide to any building committee seeking recommendations for the erection of a convalescent hospital. The book has apparently been printed by the photo-lithographic process whereby the plates are produced by photographing the original typed copy. The result has been that the reader experiences some difficulty in following the text, and the absence of sub-headings and the lack of varied type add to the reader's difficulties.

An Analysis of the "De Generatione Animalium" of William Harvey. Arthur W. Meyer, Professor of Anatomy, Stanford University. 167 pp., illustrated. Price, \$3.00. Stanford University Press; Oxford University Press, London, 1936.

The author, in his foreword, comments on the scant attention that the *De Generatione Animalium* has received, even from those who were specifically, and even officially, dealing with Harvey's life and work. He has set himself to remedy this state of affairs, and in this valuable little book has given us a critical analysis and commentary on that aspect of Harvey's work which probably interested the latter more than any other subject, not excluding even the circulation of the blood.

Complete Facts About the Colon

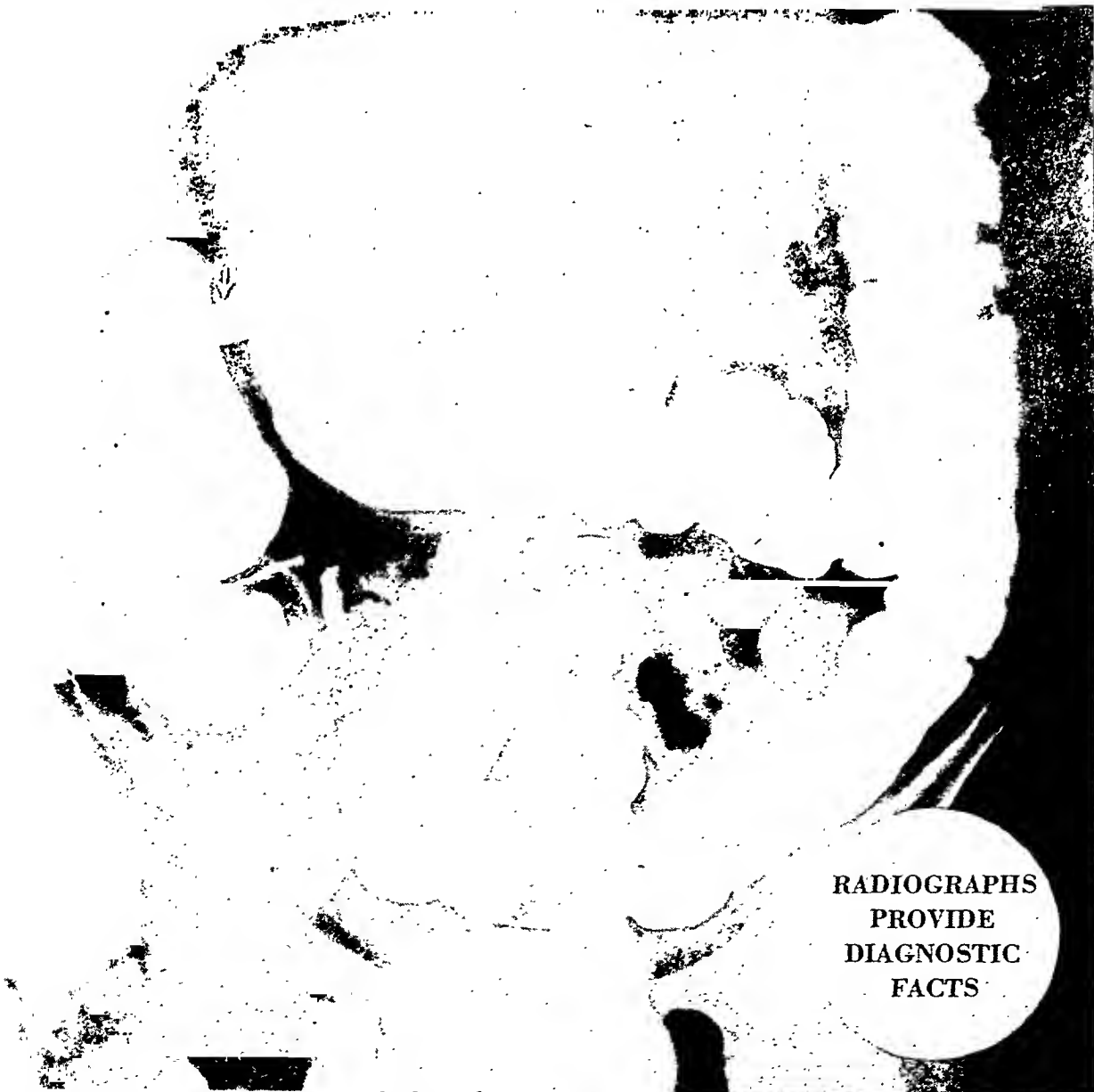
CARCINOMA is the most common tumor of the large bowel. It usually occurs in the rectum (60%), the cecum, or the pelvic colon, although it may be found in the ascending colon and the transverse colon or in the hepatic flexure and the splenic flexure.

Examination of the gastro-intestinal tract with the opaque meal administered by mouth may not show definite indications of this condition. But when the opaque enema is employed, positive information concerning alterations in contour in the tumor area may be

obtained. Therefore, the opaque enema always should be made an integral part of the complete routine examination of the gastro-intestinal tract.

Other conditions of the colon that may be disclosed radiographically are: chronic ulcerative or mucous colitis, amebic dysentery, tuberculosis, polypi, diverticula, volvulus, obstructions, anomalies, stasis. Diagnosis of gastro-intestinal involvement cannot be considered complete unless a comprehensive x-ray examination has been made by a competent radiologist.

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**RADIOGRAPHS
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importance in the actual care of the sufferer from the disease, as well as efforts to prevent the spread of the disease to others.

The general introduction clears up and accurately explains many terms which have been improperly used by many of us. The chapter on Serum Reactions should be read by all practitioners, particularly so because of the greatly increased uses of serums in treating diseases today. Many accidents, rapid and tragic, will be avoided if a study of this chapter alone be carried out. The appropriate treatment, should trouble occur, is satisfactorily given. The author has introduced each disease fully, and dwelt on the major points of each with clearly stated facts. One is struck with the complete elimination of all unnecessary enlargements. In discussing treatment each step is given, and where disagreement exists among leading physicians as to the appropriate treatment to be used all the points are set before the reader for his own decision. Sometimes this has been carried too far. In mentioning the treatment of poliomyelitis, specific serum treatment is practically thrown out as being useless. Since we have nothing better to offer, and since large quantities of specific serum have never been available, further study should be submitted. No evidence of harm has been advanced, and if possible, since there is a possibility of some help, moderately large transfusions and large quantities of specific serum should be tried, particularly from the standpoint of prophylaxis for exposed persons and for isolated cases in the pre-paralytic stage. On the whole this text can be highly recommended to anyone anxious to bring his knowledge of all the recent advances in the study of the diseases discussed up to date.

Surgical Emergencies in Children. H. C. Edwards, M.S.(Lond.), F.R.C.S., Surgeon and Lecturer in Surgery to King's College Hospital, London. 274 pages, illustrated. Price \$3.75. Baillière, Tindall & Cox, London; Macmillan, Toronto, 1936.

This small volume is based on the clinical material of the Evelina Hospital, London, and presents in a very practical way the best methods, in the author's opinion, of dealing with many of the acute surgical emergencies of childhood. Among the subjects considered are pre-operative preparation, local and general anaesthesia, blood transfusion, treatment of shock, pyogenic infections, burns, fractures, injuries to muscles and tendons, acute infections of bones and joints, head injuries, injuries and inflammatory conditions of the abdomen, empyema thoracis, injuries of the thorax, infections and injuries of the genito-urinary tract, and emergencies in the ear, nose and throat. The text is lucidly written. The author's long experience in dealing with surgical lesions of childhood gives added value to the methods of treatment which he adopts. For the surgeon who has to decide which method of treatment to follow this volume should be of much assistance.

Painful and Dangerous Diseases of the Ear. R. R. Woods, M.B., F.R.C.S.I., Surgeon in charge of Ear, Nose and Throat Department, Sir Patrick Dun's Hospital, Dublin. 188 pages, illustrated. Price \$4.50. Oxford University Press, London; MacAinsh, Toronto, 1936.

This book is essentially a reproduction of a series of clinical lectures delivered annually to the students of Sir Patrick Dun's Hospital. It does not attempt to cover the whole of the specialty, but has picked out the diseases of the ear which are of everyday clinical importance. The purpose is to give the students a

knowledge of the ear conditions with which they will have to deal in general practice. Part I is devoted to anatomy, methods of examination, and minor treatments. Part II covers Otitis Externa; Acute and Chronic Suppurative and Non-suppurative Otitis Media, including Acute Otitis in Infants. Part III covers Acute Mastoiditis, and Part IV, Intracranial Complications. It is a book which should be of use not only to students and general practitioners but also a useful guide to anyone teaching this subject.

Allergy of the Nose and Paranasal Sinuses. F. K. Hansel, M.D., M.S., Ass't. Professor of Clinical Otolaryngology, Washington University School of Medicine. 820 pages, illustrated. Price \$11.00. C. V. Mosby, St. Louis; MacAinsh & Co., Toronto, 1936.

The scheme of this work is well conceived. The opening chapters deal in turn with The Physiology of the Nose; the Biochemistry of the Sections of the Nose and Paranasal Sinuses; Cellular Reactions of the Tissues in Allergy; Histology of the Nose and Sinuses in Allergy; and the Relation of Allergy to Infection. Good surveys are given of modern views and work, and otolaryngologists will find much to interest them. The succeeding eight chapters deal with Allergy generally and it is questionable whether they add anything to what has been said in the many excellent textbooks on the subject. The Nasal Manifestations of Allergy brings us back to the main subject, and there is good descriptive writing on the subject. As regards the treatment of the major allergic disease, namely, asthma, the author wisely ends on a cautious note in reviewing the relative values of allergic and operative measures. "Every case is an individual problem", he says, "which may be solved only after repeated observations and correlations of all the facts from the clinical history and laboratory findings". The book is up to date and covers the field adequately.

Prescription Writing and Formulary. Charles Solomon, M.D., Ass't. Clinical Professor of Medicine, Long Island College of Medicine. 351 pages, illustrated. Price \$5.00. J. B. Lippincott, Phila., London and Montreal, 1935.

The subject of this work is one that the author with his varied experience in hospital and private practice and as a teacher of clinical medicine and therapeutics is well qualified to discuss. He gives many hints not only on the proper method of prescription writing but also on the avoidance of using costly proprietary preparations. There are an index of prescriptions, a general index, and a number of useful illustrations. This work is recommended for students, and it will be a valuable addition to the library of the physician.

BOOKS RECEIVED

Cardiac Output and Arterial Hypertension. S. A. Gladstone, M.D. 56 pages. Price \$1.00. Copies may be obtained from the author, 2 East 94th St., New York City, 1935.

The Technique of Contraception. Eric M. Matsner, M.D. Third edition, 40 pages, illustrated. Price \$0.50. Williams & Wilkins, Baltimore, 1936.

Diet and Commonsense. Mrs. C. F. Leyel. 302 pages. Price \$1.75. Chatto & Windus, London; Macmillan Co., Toronto, 1936.

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- Salts and Their Reactions.** Leonard Dobbin, Ph.D. and John E. Mackenzie, D.Sc., Reader in Chemistry, University of Edinburgh. Sixth edition. 246 pages. Price \$1.75. E. & S. Livingstone, Edinburgh; Macmillan Co., Toronto, 1936.
- Laboratory Methods of the United States Army.** Edited by J. S. Simmons, B.S., M.D., Ph.D., Major, Medical Corps, U.S. Army. Fourth edition, 1,091 pages. Price \$6.50. Lea & Febiger, Phila., 1935.
- Elixir of Life.** Jill Cossley-Batt, O.B.E., B.S., D.Sc., and I. Baird, F.R.E.S., F.B.S.G. 116 pages. Python Publishing Co., P.O. Box 391, Toronto, 1935.
- Roentgenographic Technique.** D. A. Rhinehart, A.M., M.D., F.A.C.R., Professor of Roentgenology and Applied Anatomy, University of Arkansas. Second edition, 431 pages, illustrated. Price \$5.50. Lea & Febiger, Philadelphia, 1936.
- Synopsis of Physiology.** A. R. Short, B.Sc., M.D., F.R.C.S., Professor of Surgery, University of Bristol, and C. I. Ham, M.B., B.Ch., F.R.C.S. Second edition, 312 pages, illustrated. Price \$3.00. John Wright & Sons, Bristol; Macmillan, Toronto, 1936.
- The Single, the Engaged and the Married.** M. Chideckel, M.D. 268 pages. Price \$2.50. Eugenics Publishing Co., New York City, 1936.
- Bacterial Endocarditis.** C. B. Perry, M.D., M.R.C.P., Professor of Medicine, University of Bristol. 137 pages, illustrated. Price \$3.00. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1936.
- The Glands of Destiny.** Ivo G. Cobb, M.D. Second edition, 272 pages, illustrated. Price \$3.00. Wm. Heinemann, London; Macmillan, Toronto, 1936.
- The Human Foot.** Dudley J. Morton, Associate Professor of Anatomy, College of Physicians and Surgeons, Columbia University. 244 pages, illustrated. Price \$3.00. Columbia University Press, New York, 1935.
- The Harvey Lectures.** Delivered under the Auspices of the Harvey Society of New York, 1934-1935. Series 30, 270 pages. Price \$4.00. Williams & Wilkins, Baltimore, 1936.
- First Aid to the Injured and Sick.** F. C. Nichols, M.C., M.B., Ch.B., M.R.C.S., L.R.C.P., L.D.S., Capt. R.A.M.D., Divisional Surgeon, St. John Ambulance Brigade. Fifteenth edition, 298 pages. Price \$0.75. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1936.
- How to Live.** Irving Fisher, LL.D., Professor of Political Economy, Yale University, and E. L. Fisk, M.D., Medical Director, Life Extension Institute (1913-1931). Nineteenth edition, 361 pages. Price \$2.00. Funk & Wagnalls, New York and London, 1934.
- International Clinics.** Vol. 2, forty-sixth series. 327 pages, illustrated. Price \$3.00. J. B. Lippincott, Philadelphia, London and Montreal, 1936.
- The Patient and the Weather.** William F. Petersen, M.D. Vol. I, part 2. Autonomic Integration. 781 pages. Price \$9.00. Edwards Bros., Ann Arbor, 1936.
- Primer of Practical and Expressive Eye Signs for Use in Cases of Serious Affliction.** R. W. Bailey, M.D., C.M. 20 pages. Copies may be obtained from the author, 212 West Penn Street, Germantown, Philadelphia, Pa.
- A Short Practice of Surgery.** Hamilton Bailey, F.R.C.S. and R. J. McNeill Love, M.S., F.R.C.S. Third edition, 995 pages, illustrated. Price 28s. net. H. K. Lewis, London, 1936.
- Synopsis of the British Pharmacopœia, 1932, and of the Poison Laws.** H. Wippell Gadd, of the Middle Temple and Western Circuit, Barrister-at-Law. Thirteenth edition, 200 pages. Price \$0.75. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1936.
- Passive Vascular Exercises.** Louis G. Herrmann, A.B., M.D., Assistant Professor of Surgery, University of Cincinnati. 288 pages, illustrated. Price \$5.00. J. B. Lippincott, Philadelphia, London and Montreal, 1936.
- Aids to Forensic Pharmacy.** Arthur W. Lupton, M.C., Ph.C., M.P.S., Lecturer in Pharmacy, University of Leeds. 226 pages. Price \$1.10. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1936.
- The Surgical Technic of Abdominal Operations.** Julius L. Spivack, M.D., Assistant Professor of Surgery, University of Illinois. 718 pages, illustrated. Price \$10.00. S. B. Debour, Chicago, 1936.
- Handbook of Urology.** Vernon Pennell, M.A., M.B., F.R.C.S., Surgeon in Charge of Urological Department, Addenbrooke's Hospital, Cambridge. 224 pages, illustrated. Price \$2.25. University Press, Cambridge; Macmillan Co., Toronto, 1936.
- The Masseur's Companion.** Arthur J. Bowman, M.I.C.M., B.P.A., M.B.A.Ch., 96 pages. Price 5s. Actinic Press, London, 1936.
- Studien zur Färbung des Nervengewebes.** By Dr. Arnold Schabadasch. 242 pages, illustrated. Staatsverlage Gorkij, 1935.
- Asthma, Hay Fever and Migraine.** A Gunn Auld, M.D. 256 pages. Price 12/6d. H. K. Lewis, London, 1936.
- Endocrinology in Modern Practice.** William Wolf, M.D., M.S., Ph.D. 1018 pages, illustrated. Price \$11.50. W. B. Saunders, Phila.; McAinsh, Toronto, 1936.

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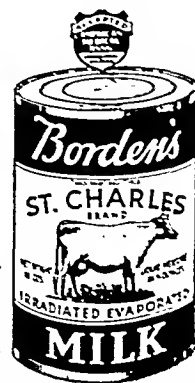
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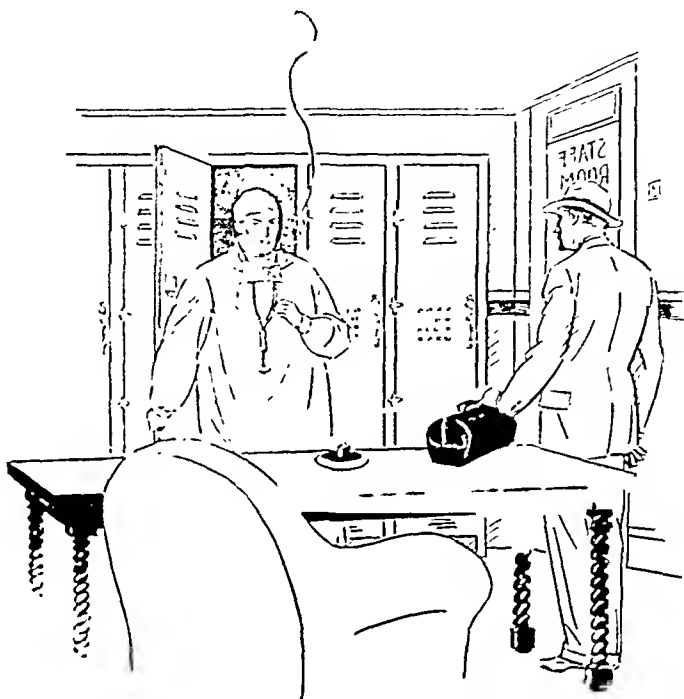
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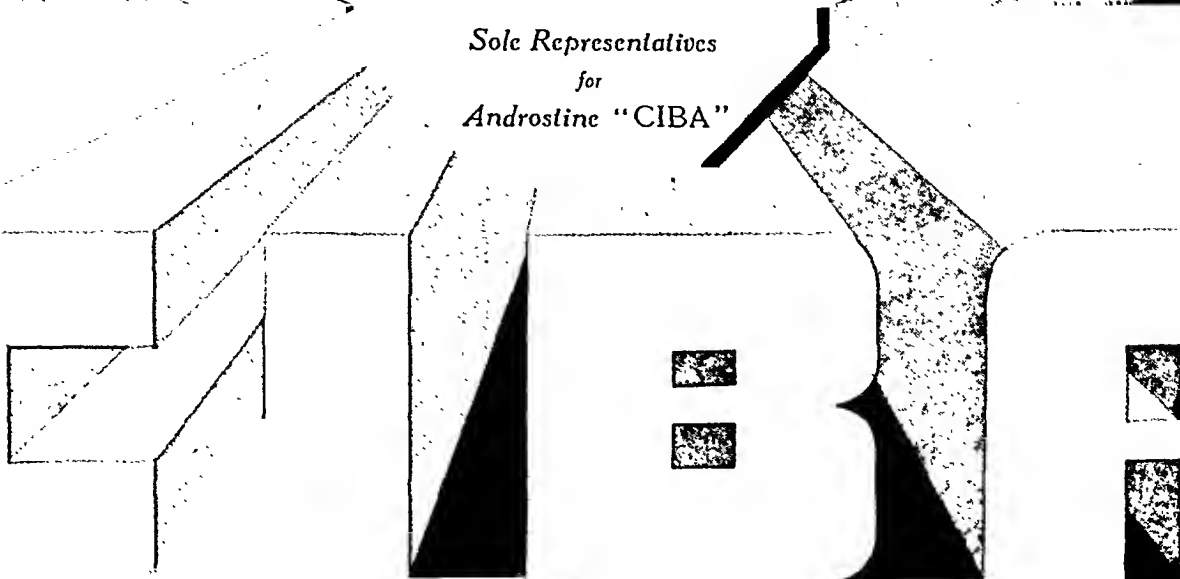


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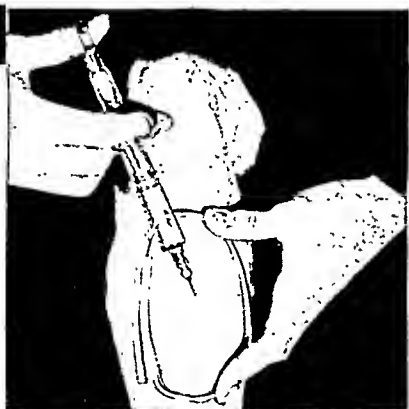
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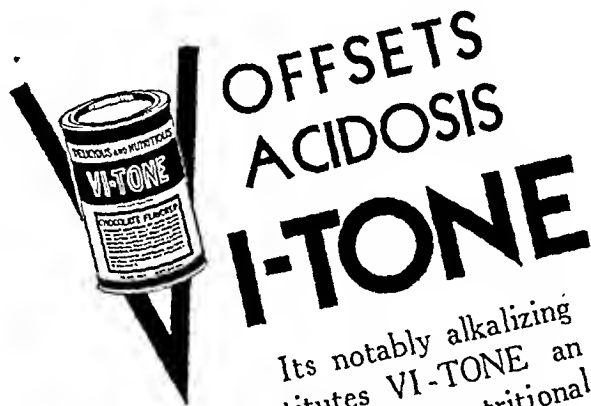
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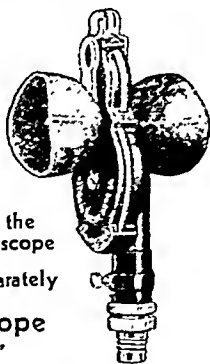
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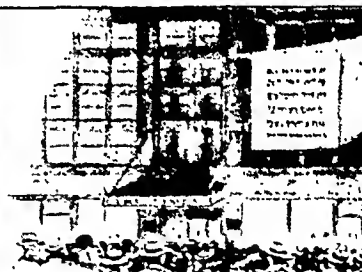
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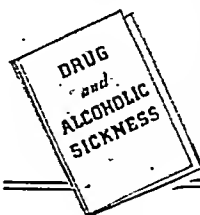
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Oral and Clinical Examinations:— October 26th and 27th at Toronto.

Annual Meeting of the College — October 31st — at Ottawa.

The subjects of the Primary Examination are:—

1. Anatomy, including Histology and Embryology.
2. Physiology, including Biochemistry.

The subjects of the Final Examination are:—

(a) For the Fellowship in Medicine:

1. The Principles and Practice of Medicine, including Therapeutics, Preventive and Forensic Medicine.
2. Pathology, including Bacteriology.

(b) For the Fellowship in Surgery:

1. The Principles and Practice of Surgery, including Operative Surgery and Surgical Anatomy.
2. Pathology, including Bacteriology.

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(a) For the Fellowship in Medicine:

1. Clinically applied Anatomy and Physiology.
2. The subjects of the *Regular Final Examination*.

(b) For the Fellowship in Surgery:

1. Clinically applied Anatomy and Physiology.
2. The subjects of the *Regular Final Examination*.

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Plastic Surgery	Sept. 16 and Sept. 17—All day. Fee £2. 2s. 0d.
Chest Diseases	Sept. 21 to Sept. 26—Brompton Hospital. All day. Fee £3. 3s. 0d.
Proctology	Sept. 28 to Oct. 3—Gordon Hospital. All day. Fee £2. 2s. 0d.
*Cardiology	Oct. 5 to Oct. 16—National Hospital for Diseases of the Heart. All day. Fee £7. 7s. 0d. (<i>Maximum of £0</i>).
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Gynaecology	Oct. 19 to Oct. 31—Chelsea Hospital for Women. All day. Fee £5. 5s. 0d.
Neurology	Oct. 19 to Oct. 24—West End Hospital for Nervous Diseases. All day. Fee £2. 2s. 0d.
Urology	Nov. 2 to Nov. 14—St. Peter's Hospital. All day. Fee £5. 5s. 0d. (<i>Maximum of 8</i>).
Medicine, Surgery and Gynaecology	Nov. 2 to Nov. 14—Royal Waterloo Hospital. All day. Fee £3. 3s. 0d.
*Venereal Disease	Nov. 23 to Dec. 19—London Lock Hospital. Afternoons. Fee £2. 2s. 0d.
Proctology	Nov. 30 to Dec. 5—St. Mark's Hospital. All day. Fee £3. 3s. 0d.
Thoracic Surgery	Dec. 7 to Dec. 12—Brompton Hospital. All day. Fee £5. 5s. 0d. (<i>Limited to 12</i>).
Dermatology	Dec. 7 to Dec. 19—Hospital for Diseases of the Skin, Blackfriars. Afternoons. Fee £1. 1s. 0d.
M.R.C.P. (Chest)	Dec. 7 to Jan. 8 (<i>excluding Christmas Week</i>)—Brompton Hospital. Two after- noons weekly 5 to 6.30 p.m. Fee £3. 13s. 6d.

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Copies of all Special Course syllabuses and of the General Course Program may be obtained on application. The Hospitals reserve the right to make any alterations necessary in dates and fees. Post-graduates are advised, therefore, to make early enquiry. Other courses are arranged from time to time, in addition to the above list.

Courses are open only to Members of the Fellowship of Medicine; the annual subscription (from the month of joining) is £1. 1s. 0d., which includes the subscription to the *Monthly Post-Graduate Medical Journal*. Overseas subscription, to the *Journal* only, is 12/- per annum, post free. Every effort is made to assist Members to obtain the post-graduate work they require.

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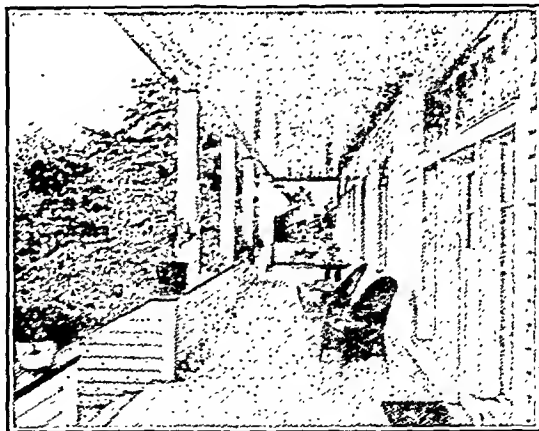
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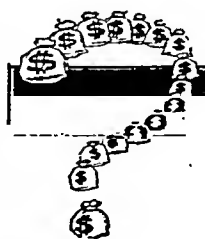
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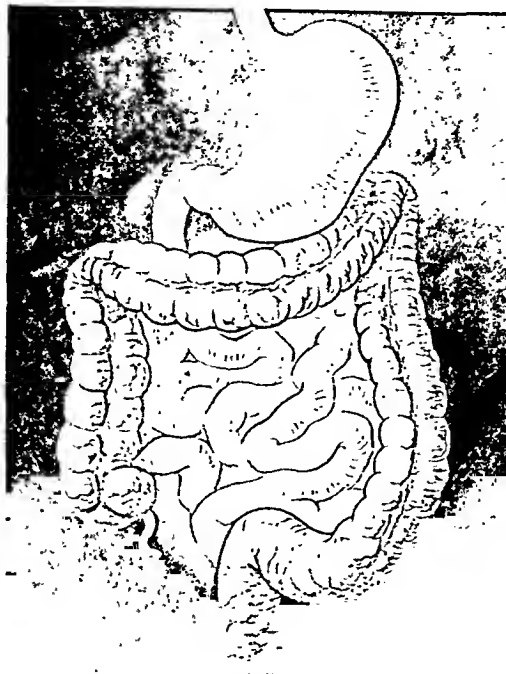
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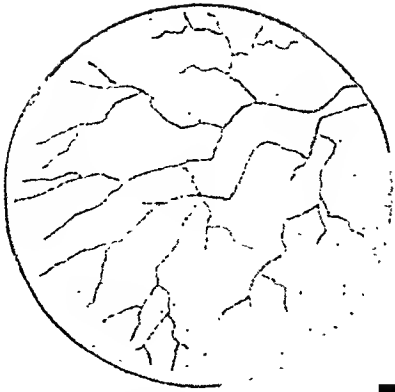
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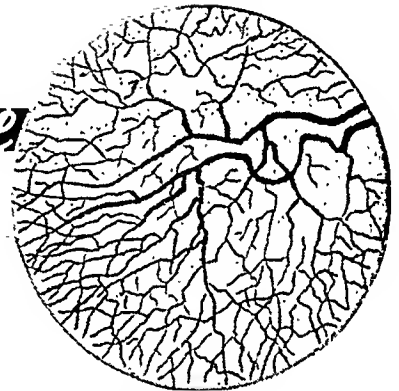
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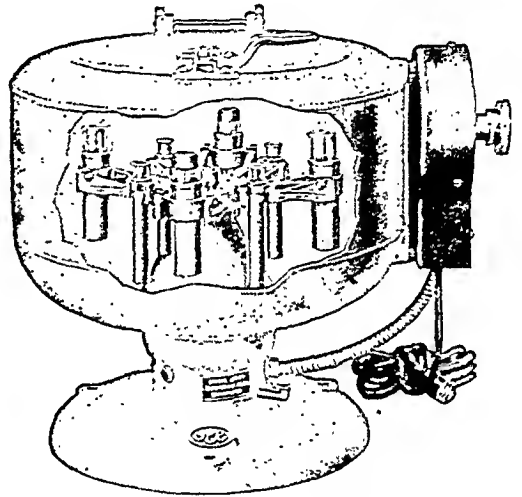
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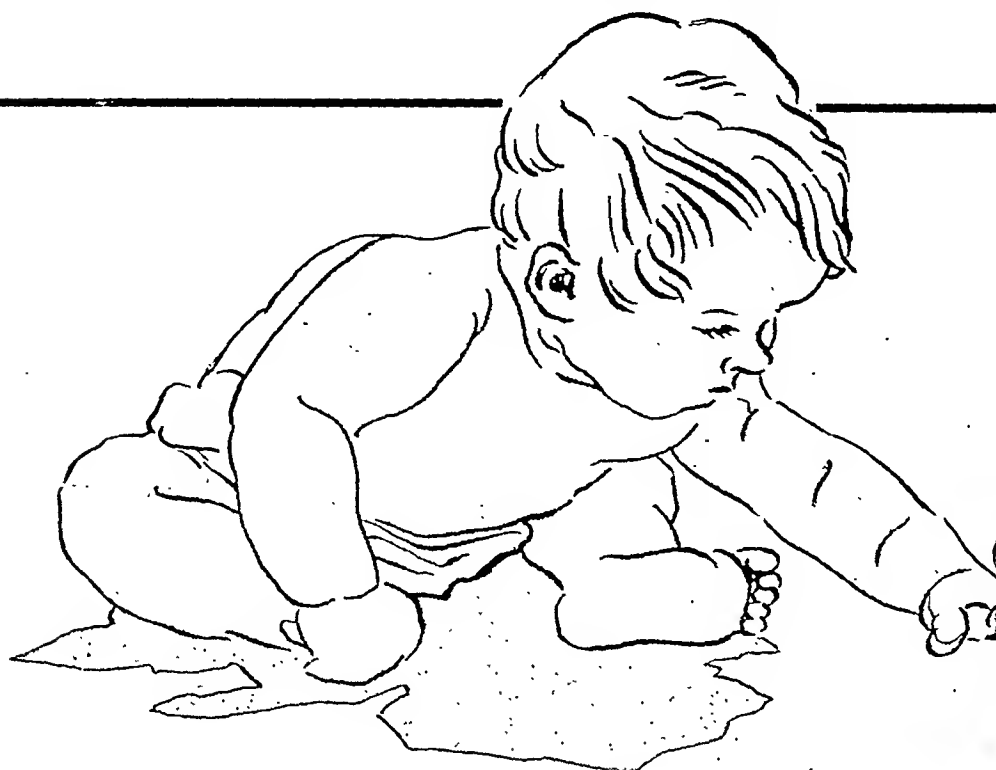
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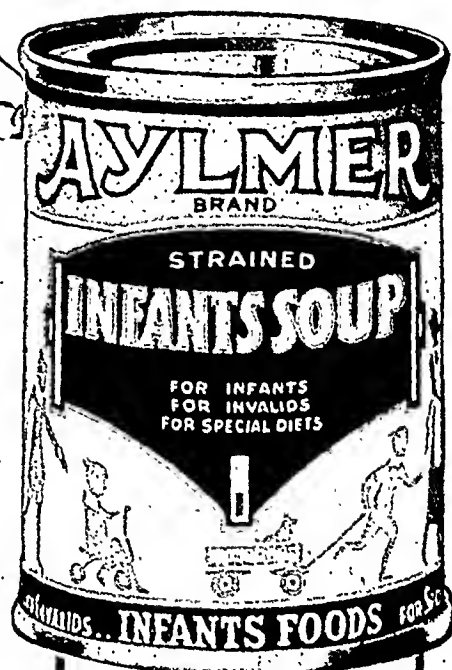
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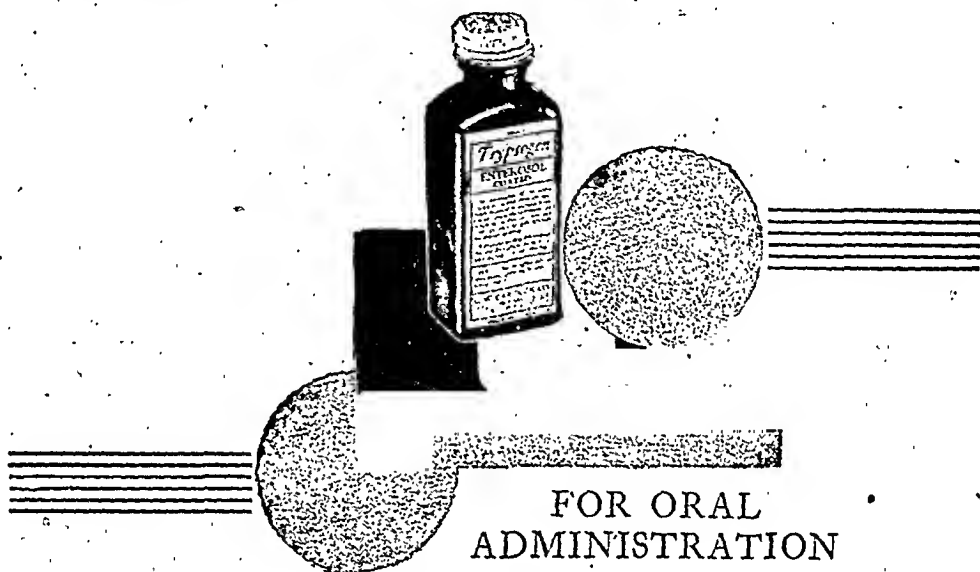
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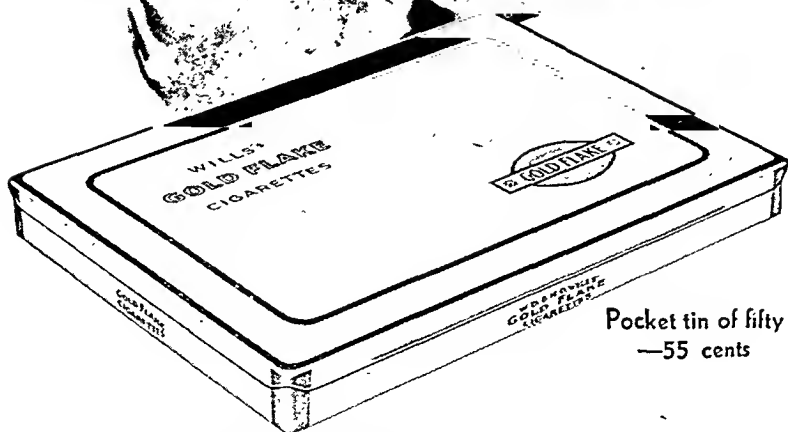
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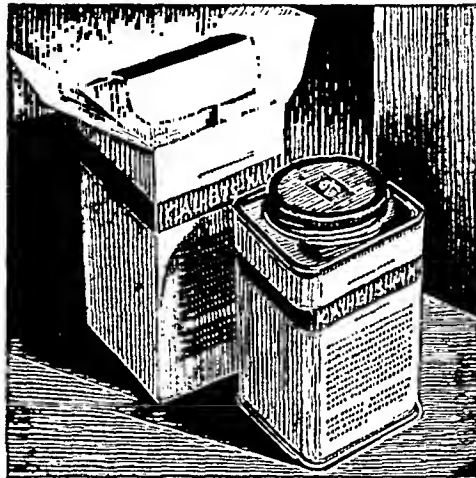
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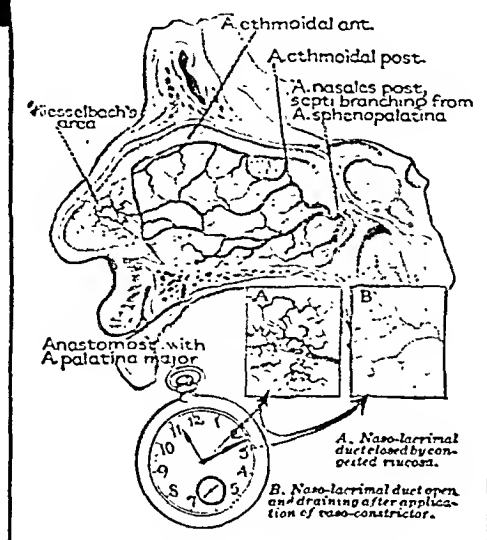
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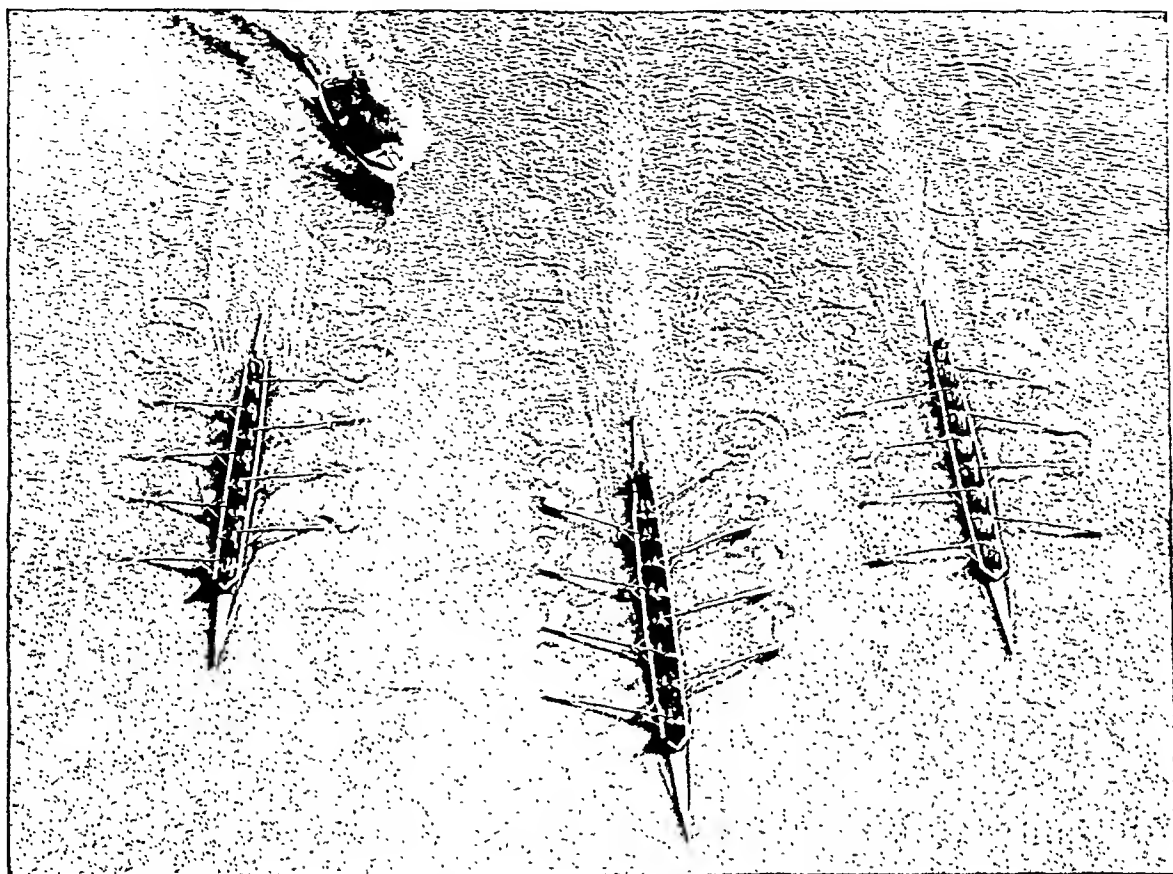
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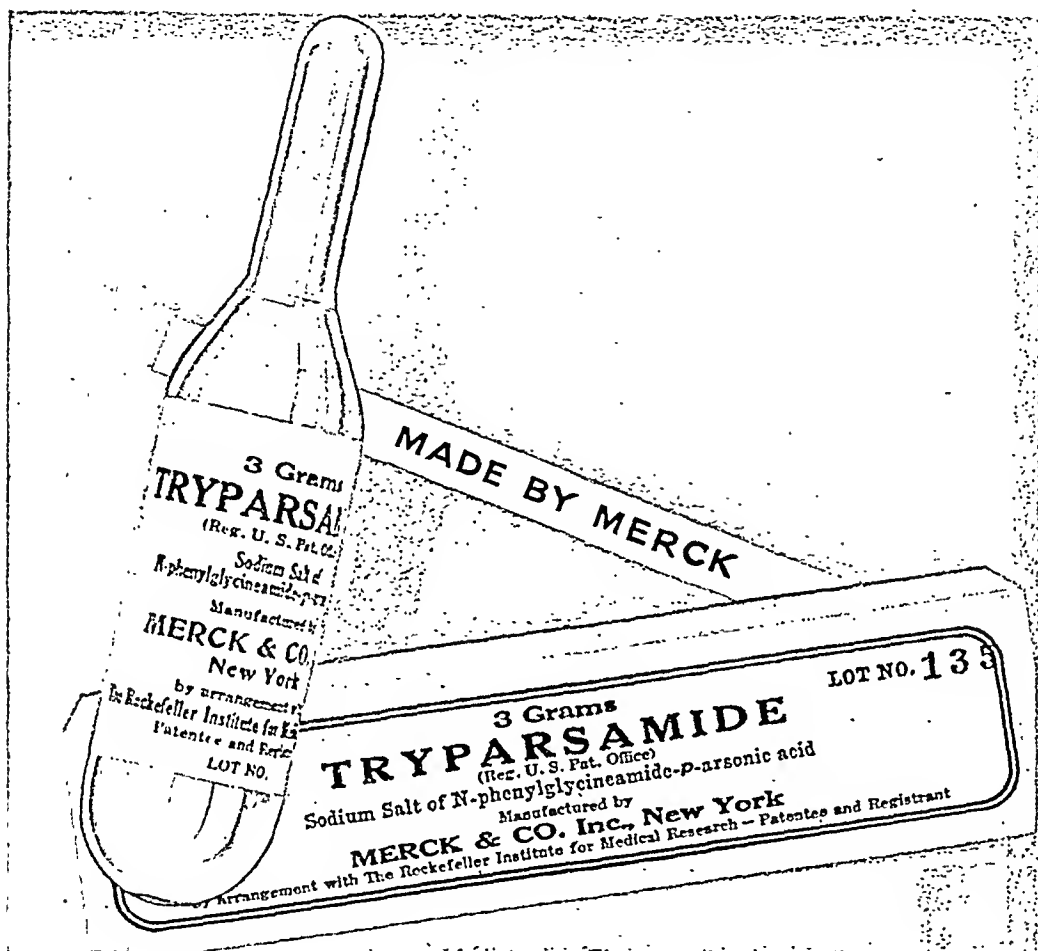
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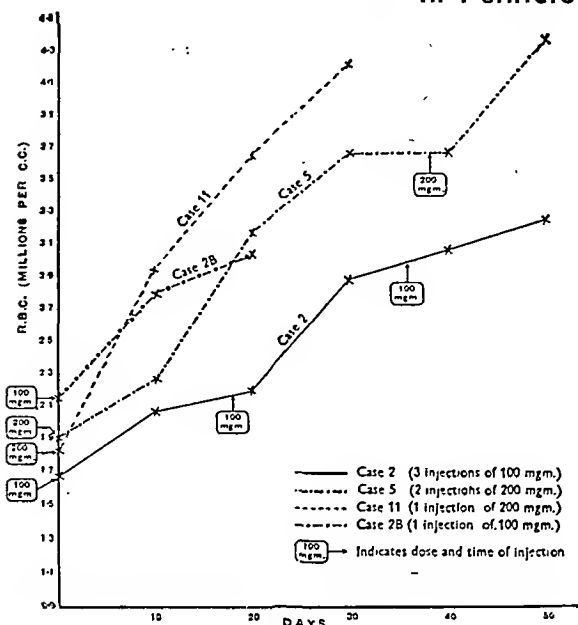
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Patch tests were made with these castile soaps and Ivory on the skins of adults, with the results shown in the following table.

Soap	Ranking
Ivory	1st in mildness
Castile A	2nd in mildness
Castile B	3rd in mildness
Castile C	4th in mildness
Castile D	5th in mildness
Castile E	6th—least mild (most irritating)

Since there were some differences among the castile soaps, the question naturally arose as to whether all of them were made from straight olive oil. A laboratory analysis showed that only two of them were made from straight olive oil while the others contained more or less of soaps from other oils. The following table shows the relative purity based on the proportion of olive oil soap in each of the castile soaps tested.

Soap	Proportion of olive oil soap
Castile A.....	0
Castile B.....	55
Castile C.....	100
Castile D.....	100
Castile E.....	70

It is significant that the mildest of these soaps is Soap A, which contains no olive oil and is very similar in make-up to the usual toilet soaps.

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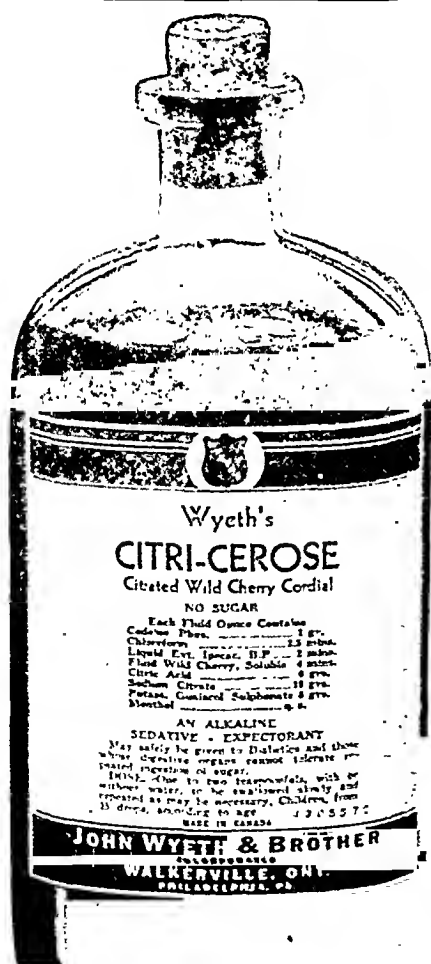
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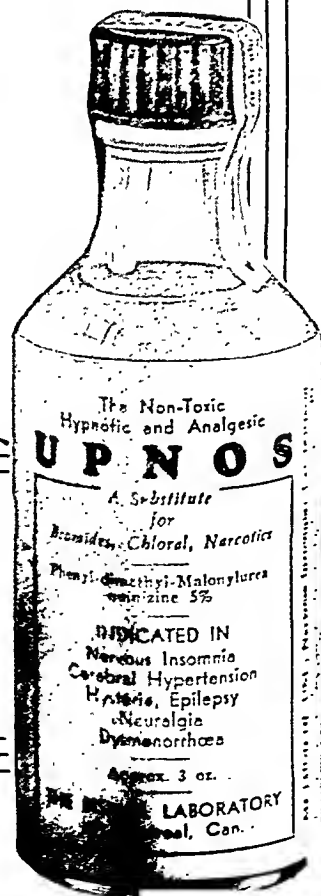
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No. 4

MALIGNANT NEPHROSCLEROSIS (MALIGNANT HYPERTENSION)*

(WITH THE REPORT OF TWO CASES)

BY LEYLAND J. ADAMS, M.D., C.M.,

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Montreal*

IN 1872 Gull and Sutton¹ condemned the narrow view which regarded kidney lesions as the primary factor in all cases of chronic Bright's disease. They referred to a constitutional form of this disease which they called "arterio-capillary fibrosis". They emphasized that in this condition there was present thickening of the arterioles (and, erroneously, of the capillaries) throughout the body, and that the kidneys merely shared in this generalized process. With the introduction of the sphygmomanometer into clinical medicine in 1893 by von Baseh² recognition of a condition now termed "essential hypertension" was inevitable. Since the classical writings of Sir Clifford Allbutt³ most clinicians have appreciated the fact that there are various degrees of severity in cases of arterial hypertension. By 1914 Volhard and Fahr⁴ divided cases of hypertension into two groups, and designated them as "benign and malignant nephrosclerosis". Later Fahr,⁵ as a result of his pathological studies, suggested that the term "malignant nephrosclerosis" be applied only to those cases in which arteriolar necrosis and endarteritis were present in addition to the arteriolar sclerosis present in nearly all instances of essential hypertension. In 1924 Keith and Wagener⁶ made a study of a selected group of patients with hypertension, in which

they felt that the clinical findings were sufficiently characteristic to establish the diagnosis of malignant hypertension. The predominant features in the majority of their cases were the sustained high blood-pressure combined with neuro-retinitis, the short duration of the symptoms, the tendency to affect comparatively young people, and the maintenance of good renal function until a late stage. They specially stressed the diagnostic importance of changes in the retinal vessels early in the disease.

We now know that in malignant nephrosclerosis one of most important and outstanding pathological changes occurs in the arterioles. These changes, while pronounced in the kidneys, occur widely scattered throughout the body—in the heart, brain, pancreas, capsule of the adrenal, gastro-intestinal tract, spleen, and skeletal muscles. They have been emphasized by all recent investigators.^{7 to 10}

While the majority of cases of so-called "essential hypertension" can be put into one large group, there are undoubtedly cases that do not fit. The term "malignant hypertension" has crept into the literature to describe this small group. There still exists much difference of opinion concerning its fundamental nature. Most authors regard it as a phase or complication of the benign essential (vascular) hypertension (Fishberg,¹¹ Christian,¹² O'Hare,¹³ Rolleston¹⁴ and others). On the other hand, Fahr⁷ and, more recently, McMahon,¹⁰ consider malignant hypertension to be a separate and distinct clinical and pathological entity.

* From the Medical Services of Dr. A. H. Gordon, and of the late Dr. C. P. Howard, and the Pathological Department of the Montreal General Hospital.

This paper is reported in part in "Medical Papers Dedicated to Dr. Henry A. Christian, Feb., 1936."

The occurrence of malignant hypertension must still be regarded as a comparatively rare condition. As a result of an increasing interest in it and knowledge of the pathological changes which characterize it we feel that in the future it will more frequently be recognized clinically. This belief is strengthened by the conviction that a more careful investigation of these cases will make it possible to distinguish malignant hypertension from benign hypertension on the one hand, and from chronic glomerulo-nephritis on the other. We have had the opportunity of studying two cases which illustrate this contention.

CASE 1

(M.G.H. No. 6610-33), a Canadian housewife, aged 42 years, was admitted to the Montreal General Hospital, into the service of Dr. A. H. Gordon, on November 7, 1933, complaining of precordial pain and shortness of breath of five years' duration, and loss of weight of six months' duration.

Family history.—Her mother died at the age of 54 years, from "sudden heart failure".

Past history.—Appendicectomy was performed at the age of twenty-one. Her only pregnancy terminated in a miscarriage at seven months. Otherwise the patient had always enjoyed excellent health and lead a very active, even strenuous life.

Present illness.—She was perfectly well until five years prior to admission, when she had attacks of bronchitis, and, after coughing, severe precordial pain which was referred to the left side of the neck and down the left arm. Associated with this pain there were marked shortness of breath and a sensation of suffocation. Ever since that time she had had repeated attacks of pain and shortness of breath, especially after exertion. Walking up steps, cooking or doing housework would often precipitate an attack. During the past three years these attacks had increased in frequency and intensity. Even the slightest exertion would bring one on. For a year before entry she was unable to do any work, and attacks occurred while at rest. Weakness became marked, and she lost thirty to forty pounds in weight. Two weeks before admission she became extremely short of breath and noticed swelling of the legs.

Physical examination revealed a well developed, well nourished woman, weighing 160 pounds, with obvious respiratory distress but no cyanosis. There was strong visible pulsation of the neck vessels. The pulse was rapid, 120 per minute, regular with good volume and high tension. The blood pressure was 260 systolic, 160 diastolic. The apical heart impulse was diffuse, visible, and palpable in the fourth and fifth interspaces, 15 centimetres from the midsternal line. In addition there was a double thrust at the apex giving a triple rhythm. The heart was greatly enlarged to percussion and by x-ray. There was a loud apical systolic murmur, and at the base both aortic and pulmonary second sounds were accentuated. Numerous râles were heard at the lung bases. The edge of the liver could just be felt. There was moderate pitting œdema of the lower legs. The ocular fundi showed slight bilateral papillœdema, numerous hæmorrhages and white spots, as well as marked sclerosis of the arterioles.

The temperature was normal. The pulse averaged 100. The specific gravity of the urine varied from 1012 to 1022; albumin was present in large amounts (three plus); no glycosuria. Microscopically there were 2 to 4 red blood cells and 4 to 6 white blood cells per high

power field, and a moderate number of hyaline casts. The red blood corpuscles numbered 4,800,000; leucocytes 8,700 per c.mm.; hæmoglobin 84 per cent (H), and the differential count was normal. The blood and spinal fluid Wassermann tests were negative. The six-foot x-ray plate of the heart showed enlargement of the heart without widening of the aortic shadow. An electrocardiogram showed a left axis deviation with depression of the S-T interval in leads one and two. Blood urea nitrogen was 22, creatinine 1.96, and blood sugar 153 mg. per cent. The basal metabolism was plus 22.

Clinical course.—The systolic blood pressure fluctuated between 220 and 270, the diastolic between 120 and 160 mm. of mercury. The œdema of the ankles and the râles at the lung bases disappeared within a few days. Dyspnea and precordial pain were the main complaints. Twelve days after admission a renal test meal showed a maximum variation of specific gravity of eight points, with no increase in the night volume. Headache, loss of appetite and nausea later became prominent symptoms. Three weeks after admission she suddenly complained of blurred vision and intense severe headache. Fresh retinal hæmorrhages and increased papillœdema were noted. A lumbar puncture revealed increased cerebrospinal pressure (500 mm. of water). A phlebotomy of 500 c.c. gave some relief, but 2 days later, she became dull and drowsy mentally. A pericardial friction rub became audible and the blood urea nitrogen had risen to 56 mg. per cent. From this time on the patient failed rapidly. The friction rub persisted; the breath became foul; the blood urea nitrogen mounted steadily to 158 mg. per cent, with the creatinine 8.10 mg. per cent. (See Chart). The respirations became Cheyne-Stokes in type. She developed convulsions and died in uræmia on December 18th, forty-eight days after admission.

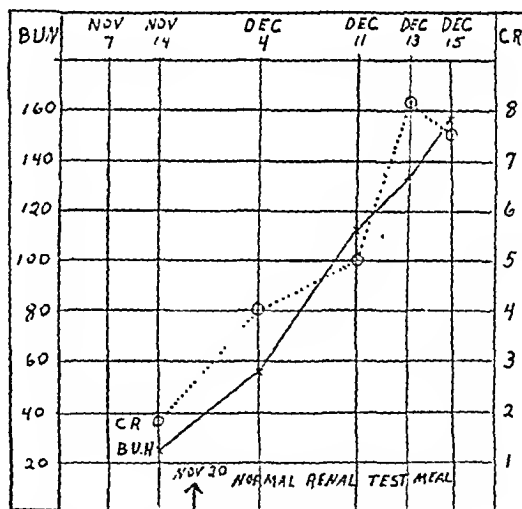


Chart showing the rapid rise in blood urea nitrogen, and creatinine.

Abstract of post-mortem record (M.G.H. A-33-256). The heart was markedly enlarged, weighing 600 grams. This was due chiefly to a concentric hypertrophy of the left ventricle, the wall of which was 2 cm. thick, while that of the right ventricle was 0.5 cm. The visceral pericardium was covered with a moderate amount of shaggy yellowish, dense, fibrous exudate. The valves appeared normal and the coronary arteries were patent.

The kidneys appeared of normal size, or even slightly larger; each weighing 165 g. The capsule was stripped with some difficulty, exposing a finely granular, deep red surface. On gross section the differentiation was good, and there were well preserved cortical striations. The cortex measured 0.5 cm. in thickness. There were no petechial hæmorrhages.

The aorta was free from any evidence of atherosclerosis, as were also the iliac, renal, splenic and cervical arteries. The lungs, liver, spleen, gastro-intestinal tract showed moderate congestion, but were otherwise not remarkable. The brain was not obtained.

On microscopic examination the blood vessels of the pericardium showed marked congestion, and there was a zone of fibrin deposit upon its outer surface. The muscle fibres were greatly increased in size. Scattered throughout the myocardium were several large and small haemorrhages, areas of myocardial atrophy, and a few foci of round-cell infiltration. One large coronary artery showed early atheromatous changes, and one smaller artery showed hyperplastic thickening of the intima. The following description is a composite picture of the lesions in the kidneys. It is based upon the examination of a series of sections taken from blocks removed from various locations and stained with haematoxylin and eosine, Masson's trichrome, Mallory's phosphotungstic acid haematoxylin, Weigert's elastic tissue stain, azan carmine, scarlet R, and stains for amyloid.

"The capsule is smooth. The glomeruli show a variety of pathological changes. A good many are atrophic, some showing partial and others complete hyalinization of their tufts (Fig. 1); while still others appear normal. An occasional glomerulus appears swollen, stains poorly, and shows red blood cells in Bowman's space. A few better preserved glomeruli also show red blood cells in Bowman's space. The azan carmine stain demonstrates a marked thickening of the basement membrane of many of the glomerular

vessels. The larger arteries show comparatively little change; those of medium size show hyperplasia of the walls and reduplication of the internal elastic membranes. The smallest arteries, and especially the arterioles, show a very marked thickening of their walls with resulting narrowing of their lumina (Fig. 2). This becomes a very striking feature in the sections stained with scarlet R. The lesion is especially marked in the afferent arterioles (Fig. 3). There are quite numerous small, irregularly distributed areas of focal necrosis and cellular infiltration somewhat resembling an inflammatory process. These areas are similar to those described by Fahr (Fig. 4).

"In some areas the tubules are dilated, in others they are atrophic and show an increase in connective tissue about them. These two changes are not, however, a striking feature. Scarlet R stains demonstrate marked fatty degeneration of the tubules.

"Lesions of the arterioles similar to those in the kidneys are seen in the spleen, pancreas, peri-adrenal tissues, and in one vessel of the lung."

The pathological diagnosis was as follows: malignant nephrosclerosis; hypertrophy of the heart; exudative pericarditis; congestion and oedema of the lungs (terminal); congestion of the abdominal viscera (terminal).

At the post-mortem one of the kidneys was removed with the renal artery intact, and injected with 20 per cent bismuth oxychloride in 10 per cent gum acacia, according to the method described by Hill.¹⁵ X-ray showed the so-called "barren fig-tree" appearance (Fig. 5).

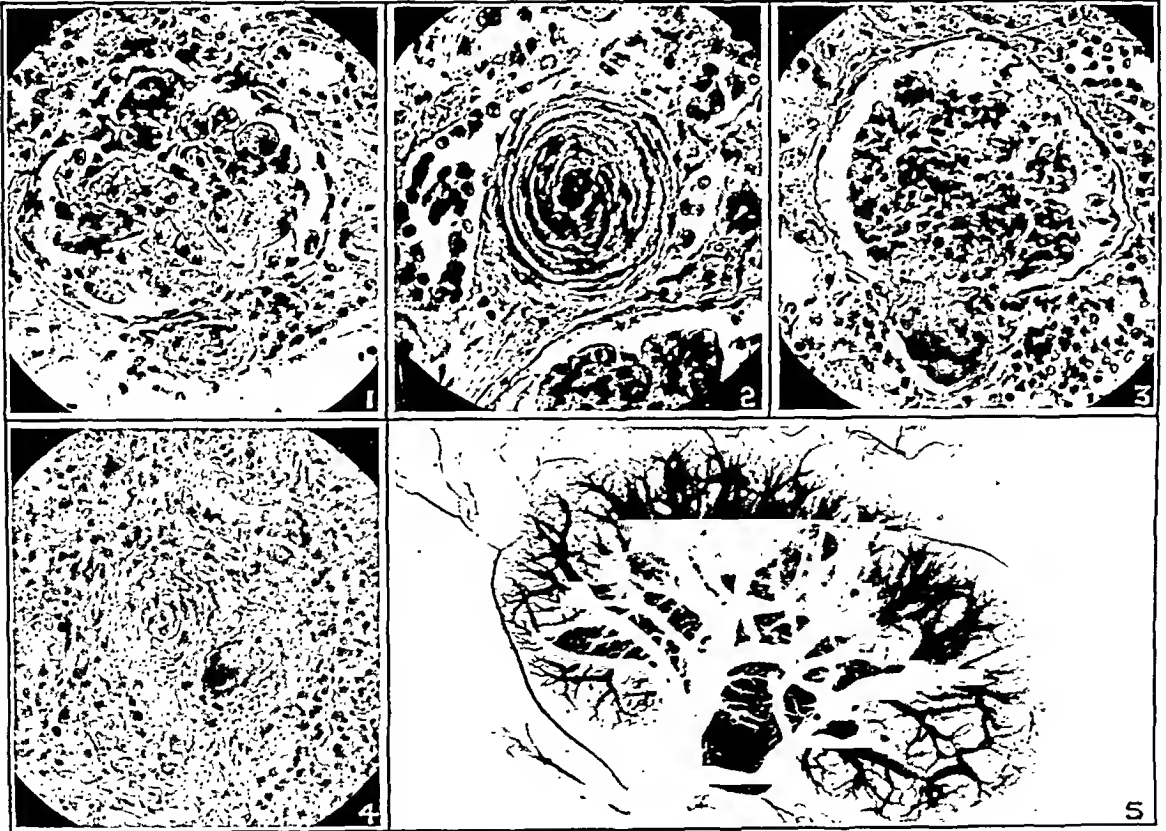


Fig. 1.—Glomerulus showing thickening of the tuft arterioles. Areas of vascular hyalinization. Fig. 2.—Arteriole showing marked thickening of the wall with narrowing of the lumen. Fig. 3.—Glomerulus showing atrophy, albuminous material in Bowman's space, and very extensive lesion of the afferent arteriole. Fig. 4.—Focal area in the kidney substance showing acute necrosis and cellular infiltration. Fig. 5.—X-ray of kidney, after its injection with bismuth oxychloride. Note the so-called "Barren Fig-tree" appearance, and abundant peri-renal arterial branches.

CASE 2

(M.G.H. No. 1166-36).—A Canadian housewife, aged 51 years, was referred to the Montreal General Hospital, by Dr. Alan B. Hall, on February 28, 1936, complaining of vomiting, dimness of vision and dyspnoea of only one month's duration.

Family history.—Irrelevant.

Personal history.—Apart from measles as a child, the patient always enjoyed good health. Married at thirty-four, two children alive and well, two miscarriages.

Present illness.—She was perfectly well until four years prior to admission, when at the age of 47 years she stopped menstruating and began to suffer from "barking noises" in the ears. At this time she was told that her blood pressure was high, over 200 systolic. One year before admission, she noticed that she became fatigued more easily and was unable to do her ordinary housework. One month before entry, she began to feel nauseated and at various times vomited repeatedly. About this time she became extremely restless and for the first time noted dimness of vision. One week before entry she consulted an ophthalmologist who told her that she had white patches and hemorrhages in the retinae. From this time on her condition rapidly became worse. Her physician reported the blood pressure to be 238/120, the respirations to be Cheyne-Stokes in type, and urine "that boiled solid".

Physical examination revealed a middle-aged female, distinctly drowsy, lapsing into periods of semi-unconsciousness. There was marked pallor, and the respirations were Cheyne-Stokes in character. The pulse was regular, rate 104 per minute, with good volume and high tension. Blood pressure was 230 systolic, 110 diastolic. The apical heart impulse could not be located, but the heart was enlarged to percussion and by x-ray. The heart sounds were clear, and the aortic second sound was accentuated. Numerous moist râles were audible at the lung bases. The liver edge could be palpated one finger's breadth below the costal margin. The right kidney was palpable. There was no oedema of the extremities. The ocular fundi showed marked oedema of the disks, retinal hemorrhages, "white spots" and marked sclerosis of the arterioles.

Clinical notes.—The temperature ranged from 98.6 to 100 degrees Fahrenheit, and the pulse varied from 96 to 124 per minute. The urine showed a specific gravity of 1008, and albumin was present in large quantities (four plus). Microscopically, there were 2 to 5 red blood cells and 5 to 6 white blood cells per high power field, and numerous hyaline and granular casts. The red blood corpuscles numbered 2,800,000; leucocytes 13,000 per c.mm.; haemoglobin 35 per cent, and the differential count was normal. The blood Wassermann reaction was negative. X-ray showed enlargement of the heart. The arch of the aorta appeared normal in size. An electrocardiogram showed changes in the T-wave in leads I and II. Blood urea nitrogen was 73, creatinine 5.45, and the blood sugar 126 mg. per cent.

Clinical course.—The systolic blood pressure remained approximately 230, and the diastolic 110 mm. of mercury. Drowsiness, vomiting, restlessness, dyspnoea, and Cheyne-Stokes respirations were predominant features. Within two days, the blood urea nitrogen rose to 115, and the creatinine to 8.10 mg. per cent. The breath became foul. She developed muscular twitchings and died in uræmia March 5th, seven days after admission.

Abstract of post-mortem record (M.G.H. A-36-44).—The heart weighed 350 grams. There were no valvular lesions. The aorta showed simple arteriosclerosis. The left kidney, weighing 140 grams, showed a slightly granular surface throughout which were scattered numerous pin-point hemorrhagic areas. On section the cortex and medulla were poorly differentiated, and showed numerous pin-point hemorrhages. The right kidney, which was similar in size and character, was removed with the blood vessels intact, injected with 10 per cent bismuth oxychloride and x-rayed. The roentgenogram

showed almost complete absence of filling of the arterioles at the periphery, in contrast to the large arteries which were well injected. The remaining organs showed no gross lesion. On microscopic examination, the kidneys showed focal areas of hemorrhage, almost universal hyaline changes in the tuft arterioles and the afferent vessels of many of the glomeruli. The medium-sized arteries showed a hyperplastic sclerosis. A striking feature was necrosis of the walls of the arterioles and the vessels within the glomeruli as well as focal areas of necrosis within the kidney parenchyma. Hyaline changes in the arterioles of the spleen and pancreas were present. The pathological diagnosis was as follows: (a) malignant nephrosclerosis; (b) hypertrophy of the heart; (c) atheroma of the aorta.

COMMENT

While the vast majority (over 90 per cent) of patients with essential hypertension never develop renal insufficiency, the two cases here reported serve to emphasize the fact that it may occur. The first patient showed extreme hypertension, pronounced cardiac symptoms, marked retinal changes and adequate renal function; and while under observation in the hospital developed signs and symptoms of rapidly progressing renal failure, resulting in uræmia and death. The second case is in many ways very similar to the first, in that it showed extreme hypertension, marked retinal changes, and rapidly progressing renal failure, resulting in uræmia and death. Post-mortem examination in each of these cases showed the pathological findings which we consider to be those that characterize malignant nephrosclerosis.

Changes in the eyegrounds were marked in both cases at the time they were admitted into the hospital. Patient No. 2 illustrates the clinical importance of these early changes, in that she consulted her oculist because of sudden onset of failure of vision. It also stresses the necessity that all clinicians be able to recognize gross changes in the fundi. Volhard¹⁶ states "The eyegrounds frequently reveal the first sign of the fatal turn in the form of contracted arteries and the classical picture of retinitis angiospastica". Just why the clinical course of certain cases of essential hypertension should suddenly change to the malignant form has never been fully understood. Volhard adheres to the theory of circulating pressor substances in the blood. Two factors however are of importance in their bearing upon the possibility of the occurrence of this sudden change. They are, the age of the patient, and the height of the diastolic pressure. The younger the individual in whom a genuine hypertension has developed, and the higher his

diastolic blood pressure, the greater is the danger that the disease may take on a malignant course.

The prognosis in malignant hypertension is grave, and at the present stage of our knowledge the treatment must necessarily be symptomatic and palliative in character.

SUMMARY

Two cases are reported with characteristic clinical and pathological findings of malignant nephrosclerosis (malignant hypertension).

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A CASE OF ALZHEIMER'S DISEASE WITH NEUROPATHOLOGICAL FINDINGS*

By J. A. HANNAH, B.A., M.D., C.M.,

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THE case which I have to present is one of Alzheimer's disease, or early senility. The condition has been studied fairly extensively, but there are certain features, both clinical and pathological, which give rise to difficulty in distinguishing it from true senility. A great deal more study will be necessary before these two conditions, which I believe to be distinctive entities, can be definitely separated. The difficulty is accentuated because there are, at first sight, certain features in the microscopic findings which are common to both, but which, on closer observation, it seems to me, do show definite differences. Clinically, the conditions can be separated by an arbitrary age limit, but such a basis does not remove the conflict which arises when the pathologist is called in. It is with the view of trying to clear up some of these difficulties that the following case is presented.

CASE HISTORY

The patient, a female, aged 53, was admitted to hospital on August 16, 1932, with the complaints of gradually developing dementia, loss of memory, periods

of restlessness, alternating with periods of depression and occasional extreme excitability.

Family history.—No mental or nervous disease in the family nor alcoholism or drug addiction were reported in any of the members.

Personal history.—As a child, the patient was bright in school, completing her high school education. She was always adjusted socially, becoming a leader in church activities and singing in the choir. She was capable of playing several musical instruments. After graduation from high school she lived at home with her mother and sister. She was very much attached to her sister, to the extent that she wished to live with her even after the sister's marriage. Although a good mixer with the female sex, she never had anything to do with the male, and there was a tendency toward a homosexual attitude.

Medical history.—There was nothing of note in the medical history. Alcoholism, drug addiction, venereal disease, and sexual relationship were denied. There was no record of previous nervous or mental disease prior to the onset of the present illness.

* From the Neuropathological Laboratory, Ontario Department of Health and Division of Neuropathology, University of Toronto.

Read before the Section of Nervous and Mental Diseases, American and Canadian Medical Associations, Atlantic City, June 12, 1935.

She was, however, quite manageable and helped with the housework in a moderately satisfactory manner until August 5, 1932, ten days previous to admission, when she suddenly became excited for no apparent reason. She would run about the house in complete confusion, mumbling in an unintelligible manner, and laughing hysterically at times; would scream at the top of her voice for several minutes. She became abusive to her sister and brother-in-law with whom she was living, and destructive to her own clothing and articles about the house. On one occasion, she upset the dining room table with all the dishes on it. These periods would abate to some extent, but would recur, and during them she would strike anyone who came near her. She had no idea where she was or what she was doing. She was deported from the States to Fergus, Ont., where she was certified by Drs. A. Groves and F. T. Russel. She was admitted on August 16, 1932. The certificates recapitulate the foregoing history, and added that the patient had for some few days to be cared for like an infant and could not feed herself.

Mental examination.—When first admitted, the patient was deeply under the effects of sedatives. Shortly after admission, when the effects of the sedatives had worn off, she became restless, running about the ward and refusing to stay in bed. She was given appropriate clothing and allowed to be up. Mental examination was quite impossible due to the lack of intelligence, inability to speak, and excitability. Her conversation consisted of mumblings, and she responded with a foolish grin to questions, and occasionally by some little impulsive act such as grabbing the examiner's pen or his necktie. She offered physical resistance to being put to bed, and was content only to wander about here and there, keeping up the while a stream of mumblings interspersed with periods of foolish laughter. Following her admission, she showed no extreme excitability and there was no evidence of violence so long as she was allowed to wander about. It was impossible to state whether hallucinations or delusions were present or to estimate the power of her memory. It was the examiner's opinion that she was completely disoriented and did not know what she was doing. The examination was abandoned at this time. Further examination on November 15, 1932, gave the following impressions and information. "When one tries to enter into conversation with this patient, the most outstanding feature is the degree of dementia which is present and is very profound. It would appear as though she had no appreciation whatsoever as to what is going on, or what is being said to her. Any attempt to test her aphasia is fruitless."

The wandering was still present. She was unable to find her way back to her bed, and was apparently unconscious as to whether or not she had any clothing on, and she had to be dressed and fed. She was unclean in her habits. The expression was a fixed smile and never varied, and there was continued mumbling which was quite unintelligible. There was a slight suggestion of carrying out commands when asked to close her eyes or put out her tongue. When asked her name she gave it correctly and then continued to repeat it four or five times. When asked when she came to hospital she repeated the last word half a dozen times. This tendency to repetition was on some occasions quite marked. At this time the differential diagnosis was thought to lie between general paresis, frontal lobe tumour, arteriosclerosis, dementia præcox, senile psychosis.

It was thought, on account of the long history and absence of localizing signs that brain tumour was unlikely. The age and mental picture were thought to exclude dementia præcox. The blood Wassermann test and spinal fluid reaction were negative; there was no history of luetic infection and it was therefore ruled out. The degree of arteriosclerosis on physical examination was not extensive, and this was ruled out. The examiner states: "The diagnosis seems to rest with the early senile group, and the case is being considered as one of Alzheimer's disease."

Physical examination.—Weight on admission, 83 pounds. The patient looked thin and ten years older than her stated age of 53 years. Due to lack of co-operation, the examination was very unsatisfactory. It was noted, however, from fleeting glimpses of the eye grounds, that they were pale but sharply defined, and it was thought that a moderate degree of arteriosclerosis was present. Nothing significant was noted about the head and neck or the chest. In the cardiovascular system, numerous extra systoles were noted; the left border of the heart extended 9 cm. left of the mid line in the 5th interspace and 3 cm. to the right in the 4th interspace; there was a slight mitral systolic murmur. The peripheral arteries were slightly palpable. The abdomen was negative. No vaginal or rectal examination was done, because of lack of cooperation.

Cranial nerves.—The first and second could not be tested; 3rd and 4th and 6th, pupils reacted to light and accommodation; the eye movements were apparently normal, but the examination was unsatisfactory. The 5th and 7th nerves appeared normal; the 8th could not be tested, but from the various partial response to commands it appeared she could hear. The 9th and 10th were negative, as was the 12th.

Reflexes.—The biceps, triceps, patellar and ankle jerks were equal, but slightly hyperactive. The plantar reflex was normal and there was no clonus. Coordination could not be tested. Speech could not be satisfactorily tested, but the patient sometimes repeats simple words such as Kiug, King, King, or Peggy, Peggy, Peggy, but this is the extent of the conversation.

Sensation.—No cooperation could be obtained, but she apparently felt pin prick throughout.

Gait.—The patient was weak, walked in a halting fashion, which it was thought could be accounted for by the degree of emaciation present.

At a conference of the staff on October 3, 1932, the case was diagnosed as Alzheimer's disease. On November 16, 1932, the patient was presented as a case of Alzheimer's disease at an inter-hospital conference. Considerable discussion was provoked after the diagnosis, but no other conclusion was reached.

Progress notes.—On December 22, 1932, the nurse in charge of this case noted a seizure which was tonic in type. The eyes were fixed, staring upwards, and the patient was frothing at the mouth. Some time following the seizure there was incontinence. The patient was receiving sedatives to control restlessness. On January 23, 1933, a further seizure was described by the nurse, occurring early in the morning, with twitching and involuntary contractions of the muscles. At this time there was incontinence during the seizure. In neither case was there any biting of the tongue. She showed some slight sign of drowsiness following the seizure, but it was not felt that the seizure was truly epileptic. On May 10, 1933, a further seizure occurred early in the morning, but with no after-effects. On July 29, 1933, a seizure of 20 minutes' duration was reported early in the morning, when she fell to the floor. Another seizure occurred on that date two hours later, which lasted for one hour, after which the patient was quite drowsy and her pupils reacted rather sluggishly to light. There were no localizing signs and no paralysis, and the seizure was thought probably due to arteriosclerotic spasm. Because of the appearance of the attacks in the early morning a hypoglycæmic epilepsy should have been considered. A similar seizure occurred August 16, 1933, and again on August 21, 1933. A note on January 10, 1934, states: "that the patient had been gradually growing weaker from day to day and died about 1 p.m. with a hypostatic pneumonia".

Laboratory findings.—The blood and cerebrospinal fluid gave a negative Wassermann test.

Autopsy.—This was performed on the date of death. The body showed extreme emaciation and looked ten years older than the stated age.

Hypostatic pneumonia in the lungs and some degree of sclerosis in the coronary arteries, and chronic sclerotic

endocarditis of both the tricuspid and mitral valves were found.

Brain.—The brain weighed (after fixation) 825 grams. The dura was markedly adherent to the skull cap and there was some increase of cerebrospinal fluid in the subarachnoid space. The brain itself was small, and the sulci were widened and deepened.

Examination after fixation.—There was extreme atrophy of the gyri throughout, but most marked in the frontal poles. The vessels at the base showed a few atheromatous plaques, but were, generally speaking, fairly well preserved. There was some thickening of the arachnoid around the base. The whole structure appeared small. The hemispheres were separated by in-

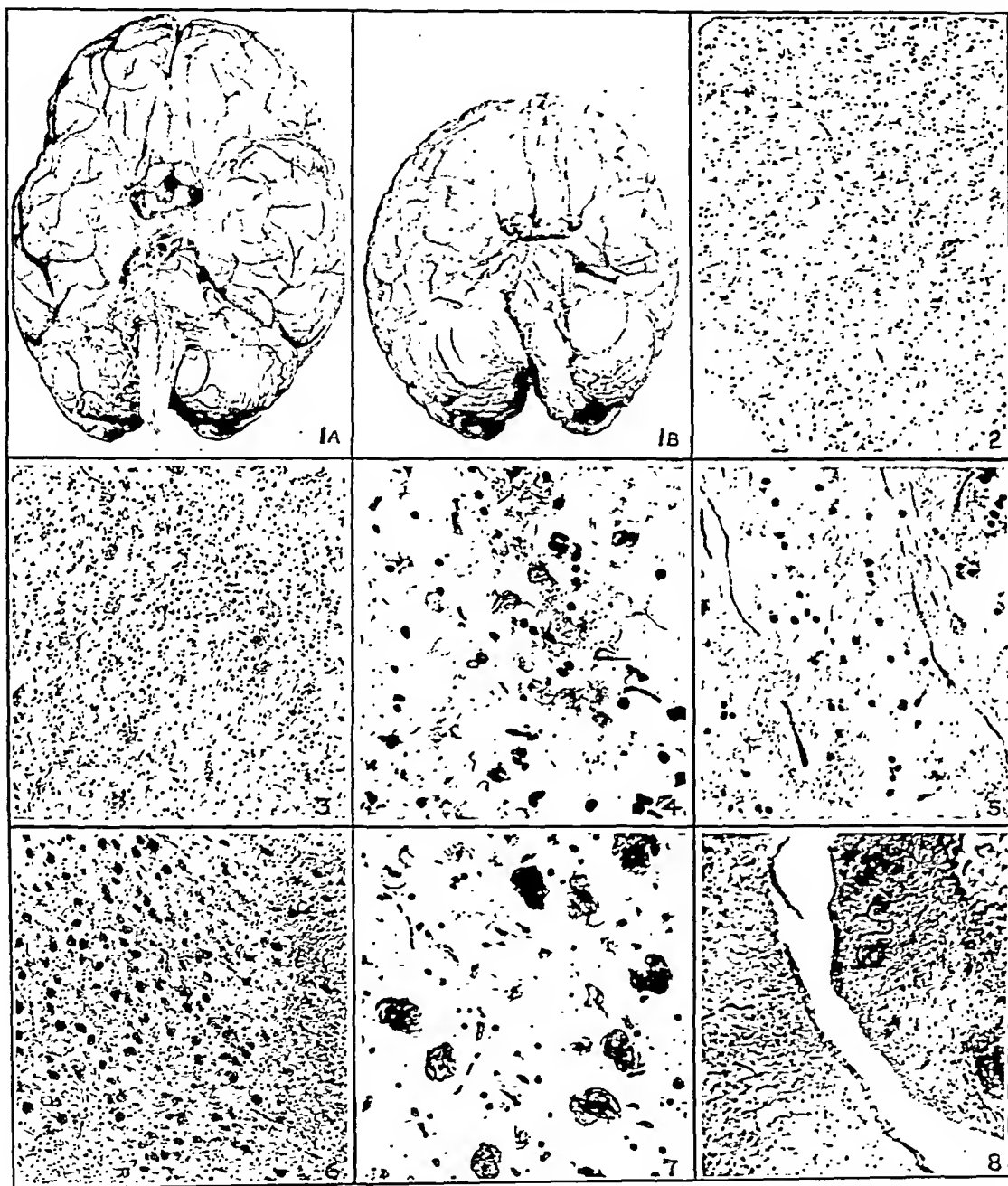


Fig. 1A.—Normal brain, weighing 1,230 grams, compared with Fig. 1B, brain from a case of Alzheimer's disease, weighing 825 grams. (Slight distortion in fixation in the brain of Alzheimer's.) Fig. 2.—Section of the cortex and white matter frontal pole, cresyl violet stain, showing extreme loss of nerve cells and degenerative processes in those remaining. Fig. 3.—L.P. Cortex frontal pole, right, Cone and Penfield's silver carbonate method, showing a large number of plaques. Fig. 4.—H.P. view of plaques seen in Fig. 3, showing plaques and Alzheimer's tangles. Fig. 5.—White matter frontal lobe, Cone and Penfield's silver carbonate method, showing secondary degeneration in neurofibrils. Fig. 6.—Nest of nerve cells in globus pallidus, L.P., showing tangles within the nerve cells. Note sharp limitation of the destructive process to the nerve cells. Fig. 7.—H.P. view of area from Fig. 6, showing tangles and early plaque formation within the nerve cells. Fig. 8.—Cerebellar cortex, Cone and Penfield silver carbonate method, showing plaques.

cision through the corpus callosum and brain stem. The atrophy of the gyri on the mesial surface was as marked as on the vertex. The pineal gland was cystic and calcified. The whole brain had a peculiar gelatinous appearance. The ventricles showed marked internal hydrocephalus. A transverse section was made through the right hemisphere, and showed a thinning of the corpus callosum and loss of white matter and thinning of the cortex. A further section made through the basal nuclei showed them to be shrunken, and there was peculiar streaking of the globus pallidus, which was sharply differentiated from the putamen. There was some streaking of the caudate nucleus as well as the globus pallidus, and the nuclei cut with considerable increased resistance to the knife.

Although the atrophy of the gyri was widespread, there was a marked lack of prominence of the frontal lobes, and the sulci in this region were much wider than in others. The frontal lobes were not only foreshortened, but were much thinner in a vertical direction than the normal brain. The whole structure, as indicated by the weight, was markedly reduced in size (see Fig. 1).

Microscopic findings.—Section of the vertebral artery, right side, showed a considerable amount of endarteritis, the lumen being reduced to half its normal size. The medial coat showed no marked changes, but there was a considerable round cell infiltration of the adventitia. The internal elastic lamina was seen to be intact, and presented the usual wrinkled appearance underneath the thickened intima. This thickening was not apparent to the naked eye in the other basilar vessels.

A section from the left frontal pole, stained with hæmatoxylin and eosin, showed some degree of thickening of the arachnoid with a slight amount of round-cell infiltration. The vessels of the meninges were somewhat engorged and at one point in the section examined there was a considerable collection of free blood in the arachnoid tissues. The cortex showed a mild increase in the surface glial tissue, the arterioles were somewhat engorged, and, very occasionally, some degree of thickening of the arteriolar wall was noted. The nerve cells were extremely rare throughout the cortex and those remaining were very degenerate in appearance. There was a relative increase in the number of interstitial nuclei noted. The white matter showed a marked increase in the number of interstitial nuclei present. Cresyl violet showed the cortex to be very thin and nerve cells are extremely scarce. Some fields showed a total absence of such cells; those which remained were pyknotic and hypochromatic in appearance, some were granular and not a normal nerve cell was seen in the section examined (see Fig. 2).

Examination of a section from the right frontal pole by the Cone and Penfield silver carbonate method showed a tremendous number of the so-called plaques (see Fig. 3). A number of compound granular corpuscles were seen throughout the cortex, and the neurofibrils were broken up and granular, and there were skein-like and basket-like forms. Under high power some of the senile plaques were seen to contain what appears to be degenerating forms of neurofibrils (see Fig. 4). Most of the plaques were seen to contain globular masses which have the appearance of cell nuclei. The remainder of the plaque was formed of granular debris. Occasionally, structures which had the appearance of degenerating fibrils could be seen lying within the plaques. The plaques were not surrounded by any process of gliosis which we could discern. There was no evidence of increase in the number of astrocytes or of glial fibres. Some of the plaques showed some degree of concentric arrangement of the granules. Some formations were noted which had the appearance of nerve cells, with granular masses which apparently represented degeneration of the intracellular neurofibrils. Only a very few normal neurofibrils were noted in any parts of the section examined.

A block from the white matter of the central portion of the right frontal pole was impregnated by the Cone and Penfield silver carbonate method, and many of the

neurofibrils were seen to be swollen, granular and irregular in outline. Nothing resembling the appearance of the senile plaques as found in the cortex was noted anywhere in this section (see Fig. 5).

A section from the basilar nuclei showed a large number of corpora amylacea in the subependymal region and region of the internal capsule. Cresyl violet stain of the basilar nuclei showed the nerve cells to be in a degenerating state, slightly less advanced than it appeared in the cortex. A block from the same region, treated by the Cone and Penfield silver carbonate method, showed definite changes within the nerve cells in the putamen and globus pallidus. These are well demonstrated in Fig. 6. They also offer a suggestion that the plaques originate in nerve cells, since they were completely surrounded by white matter, and the tangles and beginning plaques definitely were confined to the nest of nerve cells shown. Under the high power, these masses were seen to be composed of tangled skeins of neurofibrils (see Fig. 7).

A section taken from Broca's area, treated by the Cone and Penfield silver carbonate method, showed a tremendous number of senile plaques, some of which contained remnants of degenerating fibrils. Sections from this region stained with hæmatoxylin and eosin showed no structures which could be definitely called nerve cells. There was considerable engorgement in the capillaries in this region. These changes were noted in a more or less marked degree in the following additional regions: the upper end of the precentral gyrus right side; occipital pole, left side; region of Ammon's horn left side; insula on the right side. In addition, the thalamus on the left side showed a number of cells with degenerating neurofibrils and, in various regions, skein-formations. Some regions also showed an increase in the number of astrocytes. None of the typical plaque formations were noted, but some areas were very suggestive.

The cortex of the cerebellum showed quite definite plaque formations. In addition, there was some increase in the interstitial tissue; and rod-cell formations could be noted. These plaques were entirely confined to the cortical matter in the cerebellum (see Fig. 8). The medulla oblongata in the region of the olive showed some areas which were very suggestive of plaque formations.

Comment on the pathological findings.—The diffuse atrophy showed the process to have been very generalized. It would appear that this atrophy was most marked in the frontal lobes, although distortion in fixation makes it difficult to be sure. Microscopically, Broca's area showed the largest number of plaques, with the frontal lobes a close second. Clinically, mental deterioration and aphasia were early and severe manifestations. The involvement of the basal nuclei in more recent formations might suggest that the agitation and unsteadiness might have had part, at least, of their origin in lesions in this locality. The sleeplessness and loss of weight might also be linked to disturbances of vegetative functions of this area. The thalamus showed sufficient change to account for the emotional instability. From a general point of view gliosis was not a predominant feature, although localized areas were found. The wide distribution of plaques throughout the nerve cell-containing areas, and their absence in the

white matter is very suggestive of their relationship. Arteriosclerotic changes, although present in both the larger arteries and the arterioles, were no more marked than we have seen in cases showing absolutely no mental manifestations, and cannot be said to have played any very significant rôle.

DISCUSSION

Alzheimer's disease was first described by that author¹ in 1907. Up to the present time over 90 cases have been well described in the literature. Krapf² has given the most extensive bibliography, and those writers of more recent date, not mentioned by Krapf, have been noted by Rothschild.³ Numerous doubtful cases have been reported. Alzheimer's original description contains cases in the sixth decade. Perusini⁴ gave a comprehensive discourse on the disease, but he also confused it with true senility, some of his cases being in the sixth decade also. Barrett⁵ gave a description of 8 cases, but included some with histories starting in the seventh decade. The inclusion of cases beginning after the fifth decade of life, we feel, confuses the issue. In all probability such cases are of true senile origin, rather than the Alzheimer's reaction.

There are, however, many points of similarity between the two types, loss of memory, general dulling, memory retention disturbances, impairment of judgment, lack of initiative as compared with the individual's normal self, lack of interest in, and ability to concentrate on, matters formerly of interest, and disturbances of the affect tone, are characteristic of both conditions.

There are, however, certain clinical features which earmark the Alzheimer's or early type of senility. Grunthal has conveniently divided the condition into three phases.—

1. A stage of gradual loss of memory and disturbances in perception, carelessness in work and appearance, disorientation for place, weakness or epileptiform attacks, with some loss of words and slurred speech.

2. Complete disorientation for time, place, and person, dulling of comprehension, inability to read, write or do sums in simple arithmetic.

3. A stage of extreme irritability with paraphasia, uncleanness, and stereotyped movements.

The case we have reported showed all these stages. Most marked were the speech disturbances, rapid mental deterioration, and agita-

tion. The early appearance of such conditions aids considerably in arriving at a conclusion. It would seem that the "youthful senile" suffers from a loss of control over a dynamic organism, while the senile shows a deterioration of the whole organism, and pursues his downward course with an accentuation of his former personality. In the first case one system is disorganized; in the second there is slowing and degeneration of the whole anatomical structure. True, the two may overlap in symptomatology, but the one is typical of energy, misdirected, especially in the early stages, while the other is exhaustion of the whole organism from the start.

Recent workers have tended toward a distinction between these groups, both from the clinical and pathological point of view. Lowenberg and Rothschild,⁶ as well as other writers,^{7, 8, 9} have reported cases with certain basic conditions such as syphilis, and chronic infection, and offer the suggestion that the changes found in the nervous system were secondary to either infection or toxæmia.

MacDonald Critchley *et al.*^{10, 11} have attempted to distinguish microscopically, to some extent, between the plaques of Alzheimer's disease and those of true senility. Personally, we have noted that the plaques in cases of early senility and those of true or late senility have quite different appearances, those of the Alzheimer's type being much more widespread, Alzheimer's tangles are more common, and the microglial reaction is absent around the plaques. In late senility the plaques are smaller, fewer in number, and rod-cell formation around the plaque is usual. Within the limits of our experience we feel that no case having an onset after the middle "fifties" should be classified as Alzheimer's disease, unless under very exceptional circumstances. We feel also that a more thorough study of both types of cases, done under separate classifications as to age, is essential before a definite distinction can be made. Our own material is much too limited to warrant more than tentative conclusions. From what material we have seen and from the work of others we suggest that there is a distinct pathological difference between the two types of cases.

As regards the origin of the plaques, two theories have been put forward. First, that they originate from the interstitial tissue, or that they originate in nerve cells and later are added

to by the interstitial tissue. The second theory holds that they originate solely from nerve cells, and that whatever is contributed by the interstitial tissue is merely reaction to destruction of tissue and bears no relationship to the origin or formation of the plaque. In the case we have presented we have stressed the point that the plaques could only be found in those locations where nerve cells were found, and the number of plaques bore a definite direct ratio to the number of nerve cells found in any location. This we have found true, regardless of whether the case was one of early or late senile psychosis. We are therefore of the opinion that plaque formation depends entirely upon the presence of nerve-cell bodies for their formation, and that interstitial reaction is dependent upon destruction of nervous parenchyma.

CONCLUSIONS

The case presented offers a unique history of this condition. The onset of symptoms in an otherwise normal person at the age of 41, of gradual mental deterioration with loss of memory; epileptiform seizures, not characteristic of epilepsy; early aphasia, with perservation of gradually increasing severity; periods of excitability, with aimless wanderings and disorientation, all progressing to a profound degree; and eventually unsteadiness with increasing epileptiform seizures, becoming more characteristic of epilepsy, all point to the picture of Alzheimer's disease. The total duration of the disease was twelve years, which is rather longer

than usual. The pathological and microscopic findings confirm the clinical diagnosis, and are, typically, those described in the literature. So far as we have been able to learn, only two other authors have demonstrated plaques in the cerebellum, Barrett⁵ in 1911, and Rothschild³ in 1934. The appearances of the neurones in the olive were very suggestive of early plaque formations in our own case. The remainder of the central nervous system was not available for examination.

In conclusion I wish to offer my thanks to the Ontario Hospital, Hamilton, for supplying the clinical history, and allowing me to present it along with pathological studies. Dr. E. A. Linell offered some very helpful criticisms and suggestions. To Dr. Margaret S. Thompson I am grateful for her careful technical preparations, from which the photomicrographs were produced through the kindness of Dr. D. A. Irwin, Department of Medical Research, University of Toronto.

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TINNITUS.—W. J. McNALLY et al. present a study of 19 cases of tinnitus, all cases of objective tinnitus being excluded, in patients of widely different ages and with different types of ear disease; most of the patients complained more of the tinnitus than of deafness. The condition may be caused by a lesion in the nerve tissue in Ménière's syndrome by intracranial disease, and possibly by otosclerosis. However, Crowe and others did not find tinnitus a prominent symptom in cases of cochlear disease, and a study of 351 patients showed that tinnitus was present in 10 per cent without obvious local ear disease. The ages of the patients in the present series ranged from 19 to 52 years, and the duration of the condition varied from a few months to thirty years. The younger patients or those who had had tinnitus for a short period did not improve as markedly under the

various treatments as the older ones or those with tinnitus of longer duration. Ephedrine and bellafoline caused improvement in a greater number of cases when given orally than hypodermically. Stimulation of the sympathetic or depression of the parasympathetic nervous system was slightly more beneficial than the converse procedures. Stellate gangliectomy (depression or elimination of the sympathetic) produced improvement in 3 out of 4 cases. All measures were directed towards altering the cerebral circulation or cerebral pressure; the drugs used produced their full physiological effect, and they have been shown to act on the cerebral vascular mechanism. Despite the undoubted alteration of the cerebral circulation, the tinnitus in most cases was unaffected by the measures employed.—*J. Laryngol. & Otol.* June, 1936, p. 363. Abs. in *Brit. M. J.*

FILLING DEFECTS IN X-RAY PICTURES OF THE STOMACH DUE TO DISEASE OF ADJOINING STRUCTURES*

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ABNORMALITIES in pictures of the stomach due to enlargement or inflammation of adjoining structures are of course details with which the expert radiologist is quite familiar, and doubtless he may wonder at a clinician's interest in re-stating or reproducing what to him may seem merely something met with in the course of a day's work. On the other hand, in the two cases which I shall briefly describe neither expert radiologist nor skilled diagnostician seemed able to say very definitely what might be producing the rather unusual pictures which were obtained in repeated exposures. In the one case a distinctly unusual finding is recorded in association with a hypernephroma on the left kidney; in the other, a case of acute pancreatic necrosis, the pressure from fluid accumulating in the lesser sac produced a picture which puzzled all observers, a picture which, though occasionally described, is probably not often seen, since, after all, accumulations in the lesser sac of the peritoneum associated with acute pancreatic disease must very rarely come before the radiologist.

Filling defects of large areas due to extra-ventricular conditions are frequently enough described in connection with enlargement of the spleen, enlargement of the left lobe of the liver, and at times with marked distension of the gall bladder; they have been described in connection with tumours or cysts of the pancreas; and it has long been known that a tumour arising from the upper pole of the kidney or from the adrenal may produce a filling defect if it reaches high enough to press upon the posterior wall of the stomach. It has been occasionally noted that distension of a short, highly-placed transverse colon may produce a filling defect from below, as may, of course, any swelling of large size extending upward from the abdomen.

* From the Department of Pensions and National Health, Christie Street Hospital, Toronto, services of Drs. C. E. Cooper Cole and J. D. Mills.

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During the course of an x-ray examination pressure applied from the front produces a characteristic filling defect. It is usually impossible, however, to produce a similar filling defect of the stomach by pressure from behind. Pressure from sub-diaphragmatic accumulations do not seem to produce filling defects in the same ready manner as do tumour growths, and the determination of the presence of fluid under the diaphragm usually helps to explain any questionable finding in the stomach picture. Accumulations of fluid in the lesser sac of the peritoneum might tend to produce the same type of filling defect as do large tumours of the pancreas, and it would seem by no means easy to say whether in certain cases tumour or lesser-sac accumulation is producing the picture before one.

With this brief sketch of extra-ventricular conditions which may produce filling defects in the stomach it may be interesting to consider the radiological reports and the findings in two most interesting cases which have come to our notice in recent months.

CASE 1

W., aged 40, admitted complaining of weakness, epigastric pains and loss of weight of uncertain origin. It had been noted in the general examination that while lying prone a shadow could be seen to descend from the costo-vertical angle on the left side. This shadow seemed to be produced by the lower pole of the left kidney. There was nothing of a similar nature to be noted on the right side. Palpation in the area of the shadow's descent allowed one to feel a tumour-like mass, thought to be the left kidney, ascending and descending during the act of breathing. This tumour mass was considered to be the left kidney, probably displaced by some structure surmounting it, though in the early weeks of examination nothing suggestive of overlying tumour could be found. A slight deformity of the kidney pelvis could be demonstrated, a deformity suggesting pressure from above, and it could be seen that the kidney was displaced. A catheter passed easily into the left kidney pelvis. A slight enlargement of the spleen was noted, an enlargement, however, not great enough to displace the splenic flexure of the colon.

On carrying through a barium series, it was noted that as the patient lay on his back the stomach outlines were clearly defined and nothing of the nature of a filling defect showed in any screening or picture. On placing the patient prone, however, an enormous filling defect came promptly into view (Figs. 1 and 2). This filling defect needed no external pressure to produce it and remained constant as long as the patient lay upon

his stomach; it would disappear, on the other hand, the moment he was placed upon his back. The suggestion was therefore made by Dr. Thomas that in view of the evident displacement of the left kidney, as suggested by inspection and palpation and as proved by radiological picture, and in view of the curious filling defect evident in the prone position, some tumour mass, arising from the top of the left kidney, was projecting upwards far enough to fall forward on the posterior wall of the stomach and thus produce the enormous filling defect by its pressure. In no other way, was it felt, could a filling defect behaving in this peculiar way be produced. An exploratory operation some weeks later by Dr. Shenstone revealed that this was the actual state of affairs. A report on the situation of this tumour and its nature has been made by Dr. Longheed and Dr. Shenstone and will appear elsewhere. Sections showed that the new growth could best be described as a carcinoma of the adrenal. The patient died one year later with symptoms of metastases in the liver and spine.

In the production of Fig. 2, by the simple physical method of placing the patient prone some degree of undue mobility must be ascribed to the tumour springing from the adrenal. Pressure defects of similar form have been fre-

CASE 2

G., aged 42, admitted for plastic operation in connection with osteo-periostitis of the right zygoma. Within ten hours of the operation under a general anæsthetic the patient was seized with acute pain in the epigastrium, with vomiting, and with signs of great prostration. His temperature and pulse rate rose, and with these symptoms there was acute tenderness in the epigastrium. There was a very distinct rigidity in the epigastric area for a few hours, which seemed later to be replaced by a deep-seated sense of resistance. The white blood count rose rapidly, and as there had been nothing in the man's history to suggest gastric, duodenal or gall bladder disease the diagnosis of acute pancreatitis was made. The surgical consultant inclined against operative procedure, and during the next ten days a slow, gradual improvement was noted, though there still remained a feeling of deep-seated resistance in the epigastric area, an elevated white blood count, and a temperature reaching 99 to 99.5°. At this time it was considered feasible to put the patient through an x-ray examination of the stomach, though, unfortunately, at the same time he began to show signs of recurring irritation. Careful consideration of symptoms and physical signs inclined us now to believe that one of the accidents associated with pancreatitis, preferably accumulation of fluid in the lesser sac, was producing the symptoms and signs now present in this troublous case, or

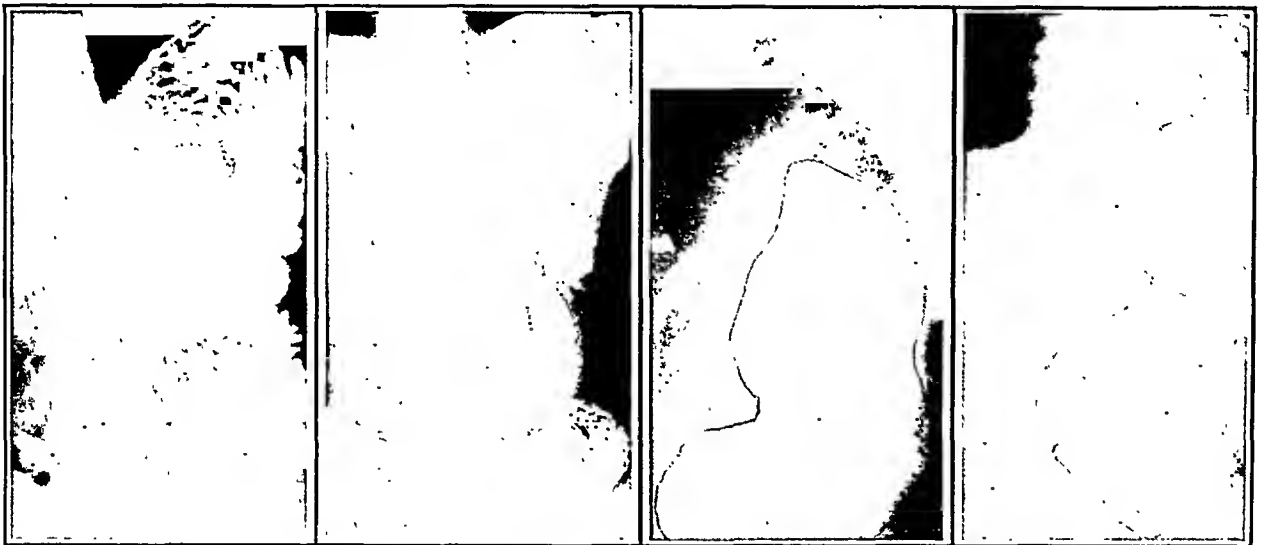


Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 1. (Case 1).—Suprarenal tumour; the normal-appearing stomach seen as the patient lies on his back. Fig. 2.—The same patient lying on his stomach. Constant filling defect probably due to falling forward of the suprarenal tumour. The filling defect remained constant in all exposures, but disappeared when the patient was placed on his back. Fig. 3. (Case 2).—Retention of the barium in the upper two-thirds of the stomach and absence of peristaltic movements. Fig. 4.—The same case. Duodenal tube *in situ*. The inability of the stomach to originate peristaltic waves and to push the barium downwards is suggested by the picture. The tube has pushed some barium over the surface of the filling defect.

quently enough described in connection with new growths of the kidney and adrenal, but they seem to have been in most instances pressure defects constant in all positions. One suggests from the report of this case that Dr. Thomas' photographs allow one to infer that a filling defect behaving as does the one we have just described is produced by a freely movable tumour springing from the adrenal or upper pole of the kidney.

that an unsuspected ulcer about the pylorus or in the duodenum was causing symptoms of obstruction by either an acute inflammation of the stomach or bowel wall or by perforating into the lesser sac. The opinion of the many consultants, both in and outside the hospital, and the opinion expressed by the majority of the latter was clearly in favour of the view that the underlying cause of the patient's trouble was a gastric or duodenal ulcer. One notes, in passing, that Dr. Carveth, senior resident of the hospital, adhered throughout to the idea that the man's illness hinged entirely upon a pancreatitis, the origin of which must remain obscure.

With the persistence of symptoms of vomiting and discomfort in the upper abdomen it was felt now that an investigation of conditions about stomach, intestine,

gall bladder and pancreas was demanded, and an exploratory operation was done by Dr. Shenstone. The stomach and duodenum were found free of ulcer, the gall bladder was distended and inflamed. There was some small amount of fluid in the peritoneal cavity, the fat of which was studded with areas of fat necrosis. The whole pancreas was involved in a process of hæmorrhagic necrosis, with perforation both into the lesser sac and through the wall of the duodenum, destroying the diverticulum of Vater and allowing fluid to pour out from the lesser sac into the duodenum. This fluid was found in large amounts when the duodenal tube could be made to pass the cardiac end of the stomach. It seemed probable from the nature of the patient's vomitus that pressure from below would force this blood stained fluid past the pylorus and lower part of the stomach, even though the cardiac end of the stomach had seemed unable, judging from the x-ray plates, to push stomach contents downwards. Little could be done to help the patient and he died five weeks after the onset of his acute pancreatitis, a pancreatitis whose complications had seemed to make an accurate diagnosis extremely difficult.

The pictures of the intestinal tract (Figs. 3 and 4), taken when first the man seemed to be improving, show findings which seem extremely difficult to explain. To the eyes of a visiting radiologist they seemed to indicate that no collection of fluid existed in the lesser sac or under the left lobe of the diaphragm. He felt that some inflammatory lesion in the walls of the stomach or duodenum, probably associated with ulcer, was giving the peculiar picture, and to this view a prominent abdominal surgeon inclined, saying that he thought the great dilatation of the stomach must be due to some obstruction in the duodenum resulting from the presence of an old ulcer. The opinion was expressed by a medical consultant that the condition was due to an acute duodenal ulcer, with œdema of the walls of the stomach and duodenum explaining the curious pictures reproduced.

Pictures very similar to those here presented are reproduced in many of the works of radiology, particularly in connection with large tumours of the head of the pancreas, and there are suggestions in many textbooks of medicine that pressure from a distended lesser sac may so affect the stomach that the x-ray picture will show a large filling defect. There are few reproductions, however, of stomach plates which show such inability of the cardiac end of the stomach to push its barium contents down into the lower two-thirds of the organ, and it was doubtless the absence of peristaltic movements and failure of the barium to be deposited below the cardia which induced consultants to think that the pictures represented an inflammatory œdema of the stomach walls. True inflammatory condi-

tions of such extent must certainly be rarely seen and the error might be held excusable. One notes that the senior resident, Dr. Carveth, early made the suggestion that the obstruction might be due to a collection in the upper abdomen, probably in the lesser sac, pressing forward and actually preventing the barium from descending. "The barium," he notes in one observation, "is still retained in the cardiac end of the stomach after 24 and 48 hours, while below this there was at one time a fluid wave which could not be made to mix with the barium in the cardia, possibly," he states, "due to a collection in the lesser sac." Since at the autopsy 500 c.c of blood-stained fluid was found in the lesser sac, and there was free connection with the duodenum allowing the entry of air into the sac, the obtaining of such a fluid wave by palpation of the epigastrium might well be possible.

A careful autopsy made by Dr. Loughheed went far to explain the nature of the peculiar radiological findings. There was a small amount of free bloody fluid in the general cavity of the peritoneum; the gall bladder was enlarged and inflamed. The left lobe of the liver was adherent to the lesser curvature of the stomach. The foramen of Winslow was blocked by the inflammatory process, which had involved the left lobe of the liver and the stomach. There was no true ulceration of either the stomach or duodenum. The head of the pancreas had degenerated into a small necrotic mass, the body and tail of this organ being the seat of a hæmorrhagic inflammation throughout which areas of necrosis were in evidence. From the head of the pancreas the necrotic process had eaten through the duodenum, completely destroying the diverticulum of Vater, and there was another perforation from the head of the pancreas into the lesser sac. Through these two perforations the contents of the lesser sac flowed freely into the duodenum. The posterior wall of the stomach reaching up to the lesser curvature was thinned and showed the effects of the necrotizing action of the fluid in the lesser sac. No distinct thickening of the walls of the stomach or duodenum was anywhere to be noted.

The conclusion to be drawn from the findings at operation and autopsy in this most tragic case, more particularly as affecting the stomach, would seem to be that both pressure from the accumulated fluid in the lesser sac and partial or complete paralysis of the musculature of the lower half of the stomach were preventing the deposition of the barium in this area.

In most of the standard works on radiology one sees references to the distortion of the stomach picture produced by tumours surmounting the kidney. One finds little or nothing, however, on the question of stomach defects caused by the falling forward of a suprarenal tumour as the patient lies on his stomach.

References to filling defects in the stomach caused by pressure of large tumours of the head of the pancreas are also readily found. One finds nowhere, however, any suggestion that

filling defects due to accumulation of fluid in the lesser sac have been observed or pictured; displacement of the stomach downwards, and as a whole, is usually reported.

CARCINOMA ORIGINATING IN SEBACEOUS CYSTS

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THE occurrence of carcinoma within a sebaceous cyst is still of sufficient rarity to justify the report of several additional cases. Rieker and Schwalbe,¹⁵ in 1914, were able to collect 43 examples from the literature. Caylor⁶ has reported the largest individual series up to the present time. It consisted of 12 instances (3.44 per cent) which occurred in 236 sebaceous cysts derived from the large volume of pathological material available at the Mayo Clinic. Bishop¹ examined 119 sebaceous cysts and found 11 (9.2 per cent) which had carcinoma present. Stone and Abbey¹⁰ found 8 malignancies (2.2 per cent) in a group of 363 specimens examined. These four reports are the largest series yet to be recorded. The remaining contributions to the literature are mainly isolated case reports.

TABLE I.

SUMMARY OF DATA PUBLISHED IN THE LITERATURE*

SEX (84 cases):			
Males	42	50.00%	
Females	37	44.00%	
Sex not stated	5	5.95%	

AGE (33 cases):

Average age in 33 patients	58.8	years
Average age in 15 males	58.0	"
Average age in 18 females	58.8	"
As reported by Caylor ⁶	58.0	"
As reported by Bishop ¹	64.2	"
As reported by Stone and Abbey ¹⁰	47.5	"

AVERAGE KNOWN EXISTENCE OF SEBACEOUS CYST (20 cases):

Males	12	10.8	years
Females	8	8.0	"

LOCATION OF SEBACEOUS CYST (58 cases):

Scalp	20	34.50%
Eyelids	9	15.51%
Nose	9	15.51%
Forehead	8	13.80%
Cheek	6	10.35%
Neck	1	1.72%
Shoulder	1	1.72%
Arm	1	1.72%
Abdominal wall	1	1.72%
Back	1	1.72%
Knee	1	1.72%

(Note: 53 (91.4%) were situated cephalad to the shoulders.)

Table I presents a summary of the available data as presented in the accessible literature upon this subject, totalling 84 instances of this pathological entity. The inferences to be drawn from the summarized data in Table I are as follows. Sex is of little significance. The patients are elderly, averaging 57.5 years of age. In 20 instances the average known existence of the sebaceous cyst had been 8.7 years. In 91.4 per cent of all of these malignant sebaceous cysts they were located upon the head or neck. In 40.0 per cent of the patients it was necessary to perform two or more operations so as to completely remove the lesion. In 34 of the reported cases, 14.7 per cent were basal-cell epitheliomas, but none of them arose from a sebaceous cyst

TABLE I.—Continued.

NUMBER OF OPERATIONS PERFORMED IN ATTEMPT TO CURE THIS DISEASE (20 cases):

	Males	Females	
Patient refused surgery	1		5.0%
One	9	2	55.0%
Two	1	3	20.0%
Three	2	1	15.0%
Four	1	0	5.0%

PATHOLOGICAL FINDINGS (34 cases):

			Deaths	Mortality
Basal-cell carcinoma (None reported upon scalp).....			5 14.7%	0 0.00%
Epidermoid carcinoma: Not classified.....			8 23.5%	3 37.50%
Group I, Broder's Classification.....			10 29.4%	0 0.00%
Group II, Broder's Classification.....			4 11.7%	0 0.00%
Group III, Broder's Classification.....			4 11.7%	1 25.00%
Group IV, Broder's Classification.....			1 2.9%	1 100.00%
Pre-cancerous lesions.....			2 5.9%	0 0.00%

RESULTS OF CLINICAL FOLLOW-UP (34 cases):

Well	24	70.60%
Not traced	3	8.82%
Died (7 cases):		
From carcinoma of sebaceous cyst	5	14.71%
From other causes	2	5.88%

*Based upon reports by Nos. 1, 4, 5, 6, 12, 13, 15, 16, 17 and 19.

situated in the scalp. This is of interest as a study of 58 of the reported malignant cases showed that 34.5 per cent had occurred in the scalp. Of the 5 cases of epidermoid carcinoma which were graded III and IV, according to Broder's classification, 40 per cent died from recurrence. Fourteen cases were graded I or II, and no deaths were attributable to a recurrence of the carcinoma. In a clinical follow-up study made upon 34 of the patients 70.6 per cent were well; 14.7 per cent had died from recurrence of the epithelioma; 8.8 per cent could not be traced; and 5.8 per cent had died from causes unrelated to their previously removed malignant sebaceous cyst.

Bishop,¹ Broders,² Caylor,⁶ MacCarty,^{10, 11} Ormsby,¹⁴ Stelwagon,¹⁸ and the Suttons²⁰ have adequately and thoroughly discussed the origin of sebaceous cysts, and have enumerated the various factors responsible for their malignant degeneration. These excellent data will not be

CASE 1

A Mexican male, aged 40, a labourer, entered the minor surgical clinic complaining of a tumour on the anterior abdominal wall which had become painful and was enlarging in size. He had noticed this mass about four years previously. Examination showed this to be cystic, measuring 2 x 2 x 1.5 cm., situated in the right lower anterior abdominal wall, which was rather firm and irregular to palpation. It was completely removed under local anaesthesia. Microscopic sections revealed the presence of an epidermoid carcinoma, grade II, growing profusely within the walls of a sebaceous cyst. Caylor found two cases (0.87 per cent) of his series of 236 instances that occurred in this same area; while one (0.43 per cent) became malignant and was diagnosed as a squamous-cell epithelioma, grade I (Case 6 of his series of 12 malignant sebaceous cysts). Fig. 1 depicts a typical area from the cyst wall showing the carcinoma.

CASE 2

A German male, aged 77, a farmer, had had a "wen" on the right side of his face for the previous seven years which periodically drained foul-smelling cheesy material. This had been cauterized by his own physician seventeen months previously. The area failed to heal entirely, and four months ago the ulcerated area began to enlarge and became indurated. When first seen the ulcerated lesion measured 3 x 3 x 1 cm., and appeared clinically to be unquestionably malignant. The entire lesion was treated by wide excision and thorough diathermy. Microscopic examination of the specimen re-

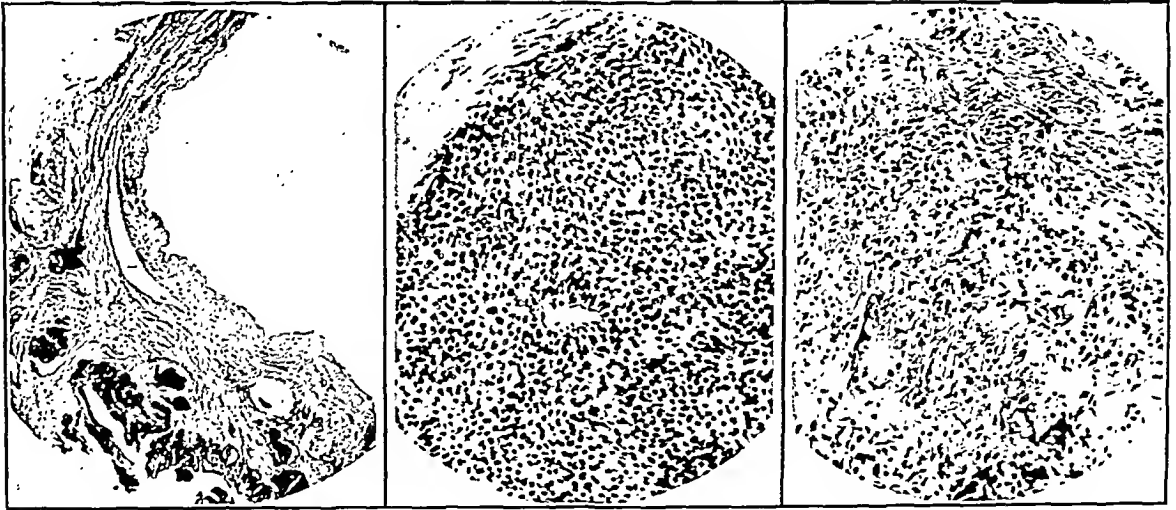


Fig. 1

Fig. 2

Fig. 3

Fig. 1. (Case 1).—Shows the presence of an epidermoid carcinoma, grade II, in the wall of a sebaceous cyst. (x13). Fig. 2. (Case 2).—Shows the histological details of the epidermoid carcinoma, grade III, in the wall of a sebaceous cyst. (x100). Fig. 3. (Case 3).—Shows definite precancerous changes in the walls of a sebaceous cyst. (x130).

repeated here. However, the reader is urged to read at his leisure the classical contribution of Caylor upon this subject. Nothing has been added to the sum of our knowledge upon this subject during the past eleven years since the publication of his article.

I wish to report briefly three examples of this pathological condition that have occurred in the routine examination of approximately 9,000 pathological specimens (0.033 per cent).:—

revealed an extensive epidermoid carcinoma, grade III, in the remnants of a sebaceous cyst. Fig. 2 is a photomicrograph of the histological appearance of the epidermoid carcinoma.

Caylor had 12 (14.71 per cent) sebaceous cysts in this location in his group of cases, and two (0.87 per cent) were malignant, being graded II and IV, respectively. (Cases 7 and 12).

CASE 3

An Austrian male, aged 45 years, entered the minor surgical clinic complaining of a cystic tumour in the palm of his left hand, situated between the second and

third metacarpals, of about five months' duration. This mass, although painless, interfered with his working as a labourer and had recently slightly enlarged in size. Under local anaesthesia, this cyst was removed in its entirety. Microscopic study revealed the presence of areas of atypical epithelial cells containing large hyperchromatic nuclei and enlarged nucleoli with an occasional mitotic figure. This microscopic picture was diagnosed as being a definite precancerous lesion in a sebaceous cyst wall. Fig. 3 is a photomicrograph demonstrating the precancerous histological appearance of the sebaceous cyst wall.

According to the Caylor series, one cyst (0.43 per cent) occurred on the palmar aspect of the left second finger, and this lesion was benign. No cases of malignant degeneration were found recorded in the literature as occurring in this location. Bishop included two instances of precancerous changes in sebaceous cysts of the scalp in his article.

SUMMARY

Three instances of malignant changes occurring in sebaceous cysts are recorded. The literature has been partially reviewed and the data obtained from this study have been tabulated. All sebaceous cysts should be considered as precancerous lesions, and they should be closely observed if the individual does not consent to their surgical removal. Increased age, long existence of the sebaceous cyst, and probably local irritation are important contributory factors in the causation of malignant changes in sebaceous cysts. These three reported instances occurred

in some 9,000 routine examinations of all types of pathological material, an incidence of about 0.033 per cent.

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MYASTHENIA GRAVIS: RESULTS OF TREATMENT IN SIX CASES*

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AS early as 1870 Rosenthal¹ pointed out that certain myopathies were associated with disturbances in creatinine excretion. In 1909, Levene and Kristeller² carried out quantitative studies on cases with myopathies which showed a definite disturbance in creatine and creatinine excretion, namely, that there was not only a low creatinine but a high creatine excretion in these cases. In 1929, Brand, Harris, Sandberg and Ringer³ showed that when glycine was fed to patients with progressive muscular dystrophy there was a definite increase in the excretion of creatine. Thomas, Milhorat and Techner⁴ (1932) repeated this work and confirmed it, but, having carried on the experiments over a prolonged

period, they observed the therapeutic effects of such administration in cases of progressive muscular dystrophy. Others⁵ claim similar results. Boothby⁶ found no clinical improvement when glycine was administered to three patients with progressive hypertrophic muscular dystrophy. However, he did note a marked improvement on giving glycine to two patients with myasthenia gravis, although a third improved very little. Since this report many other workers have confirmed the observation that myasthenia gravis is more likely to respond to glycine than other myopathies.

X-ray irradiation of the thymus gland in the treatment of myasthenia gravis was used by German workers as far back as the beginning of the century. Pierchalla,⁷ in 1921, referred to

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the various opinions as to its merits. This method of treatment has been advocated by a number of observers since that time. However, others have doubted its value on the grounds that the remissions attributed to treatment in certain cases may have been spontaneous in nature.

In 1929, Edgeworth,⁸ who is suffering from myasthenia gravis, found a marked improvement of her condition with the use of ephedrine, and since then many other favourable reports have been made concerning the use of this drug in myasthenia gravis.

Walker⁹ (1934) was impressed by the similarity in manifestations of curare poisoning and myasthenia gravis. Because physostigmine is a partial antidote for curare poisoning, she felt that it might prove of benefit to patients with myasthenia gravis. Having an undoubted case of myasthenia gravis under her care, she administered physostigmine and obtained very definite improvement in the symptoms. It was necessary to combine atropine with the physostigmine to combat the intestinal cramps. Denny-Brown¹⁰ (1935) advises 20 min. of tincture of belladonna in water by mouth, followed twenty minutes later by 1/6 gr. physostigmine salicylate in water, administered once daily on an empty stomach. This, the writer states, causes a decrease in the symptoms of myasthenia. Recently, an isomer of physostigmine, called prostigmine, has been prepared, which is more active and not so prone to produce intestinal colic. The effect of this drug on cases of myasthenia gravis is very dramatic, but, unfortunately, of short duration. This preparation may throw some light on the pathology of myasthenia gravis. It is now postulated that the effect of prostigmine is to inhibit the acetylcholine esterase in the muscle cell at the nerve ending and thus allow the acetylcholine to act upon the muscle cell.* Whether the increased stimulation of the muscle cell proves beneficial or harmful ultimately remains to be seen by further use of protigmine.

Simon¹¹ recently reported the successful use of antuitrin in two cases of myasthenia gravis, but as yet this work lacks confirmation.

CASE HISTORIES

Since 1930 six cases of myasthenia gravis have been admitted to the public wards of the Toronto

General Hospital. Several other cases observed during this period have not been included because the diagnosis of myasthenia gravis was not sufficiently definite. These six cases have been under the continuous observation of the author, and their clinical progress has been studied both in hospital and subsequent to discharge in the out-patient clinic. The clinical histories which follow are reported in some detail with particular reference to the effect of the various therapeutic agents employed.

CASE 1

Miss V. K., aged 21, factory worker, admitted to the Toronto General Hospital, October 14, 1931.

History of illness.—Three years before admission she noted weakness of her legs, particularly when attempting to mount steps. The weakness became more apparent towards the latter part of each day and was much less noticeable in the morning. By December, 1929, it became necessary to stop working, and about this time double vision developed after reading. During the six months previous to admission phonation became weak after conversing a short time. She had difficulty in chewing, and as each meal progressed swallowing required increasing effort. Her symptoms have always been much worse during the week preceding each menstrual period. At this time the weakness in her legs and back had become so severe that she had had to crawl upstairs on hands and knees. Her condition always improved quite markedly on the third day of the menstrual flow.

Examination.—The patient was a well-nourished girl with no muscular wasting. There was moderate bilateral ptosis; the lips were constantly parted, and it required obvious effort on her part to bring them together. Frequently she would support her lower jaw with her hands. No strabismus was demonstrable, but diplopia was readily produced. Extreme upward, downward, lateral movements or convergence could only be maintained momentarily. The voice was nasal, and after conversing for a few minutes it became weak and indistinct. The muscles of the trunk and limbs were all very weak, especially those of the lower limbs and trunk, and sustained effort against resistance of the various muscle groups resulted in rapid fatigue. After resting for a few minutes the power improved. Her gait was slow and of a waddling character. She was unable to walk upstairs unaided. When placed recumbent on the floor she was unable to raise herself without assistance. Apart from these findings, examination revealed nothing of significance except the blood pressure, which was 94/62 reclining, 86/62 sitting up. X-ray and fluoroscopic examination of the thymus gland revealed no enlargement. Electrical stimulation with the faradic current showed the fatigue phenomenon in the muscles of the face and limbs characteristic of myasthenia gravis.

Treatment and progress.—The patient was placed at rest in bed for six weeks and given a course of x-ray irradiation to the thymus gland. She was discharged from hospital in November, 1931, unimproved. A slight improvement was noted during January and February, 1932, but in March a very decided improvement occurred. This continued until September and during the summer she was able to take fairly long walks and to eat without any weakness developing. However, in September, 1932, she began to tire more easily and difficulty in swallowing recurred. The weakness in her limbs became increasingly severe and on re-admission to hospital in January, 1933, her body showed numerous bruises from falls sustained due to weakness in the legs. Examination at this time showed ocular muscles weak and easily fatigued, resulting in strabismus and diplopia. Ocular convergence was a weak movement which could not be maintained. There was generalized severe weakness of all facial muscles on voluntary or emotional movements. Attempts to chew

*In this connection, Drs. McVicar and Cleghorn, of the Department of Medicine, estimated the activity of the acetylcholine esterase in blood in three of our patients (Cases 1, 5 and 6) and found no consistent deviation from the normal amount of this substance in the blood.

or swallow resulted in rapid fatigue of the muscles concerned. The voice was nasal but did not fatigue as readily as formerly. The power in the muscles of all four limbs was poor, particularly in the proximal groups. The patient had great difficulty in sitting up from a recumbent posture, even when using her arms.

On January 24, 1933, glycine 5 grams thrice daily, and, twenty minutes after each dose, ephedrine, $\frac{1}{4}$ grain, were prescribed. During the next three days a remarkable improvement occurred. On January 27 she could eat her meals without difficulty, could step up on to a chair, and was free of strabismus or ptosis even at the end of the day. She noted a subjective increase in muscular power and stated that she felt stronger than at any time since the commencement of her illness. Examination substantiated this statement and it was only after prolonged repeated movements that fatigue could be produced.

In April glycine was discontinued for two weeks. A few days after stopping glycine, the patient noted that she tired more easily. Her face assumed its former appearance, with well-marked ptosis and diplopia and profound weakness of all muscles: chewing, swallowing and speech were affected. When the glycine was resumed there was rapid improvement in the power of her limbs and the muscles of expression and mastication. The diplopia improved very slowly, however. On a day when she felt exceptionally well a duodenal tube was passed for experimental reasons. Although this did not distress her much at the time, extreme weakness developed in a few hours. Her condition gradually became worse and she was so weak the following day she could hardly move her limbs; her face was very myasthenic in appearance, and she complained of headache and vomited several times. The weakness persisted for three weeks, and then gradually recovery occurred so that she was discharged from hospital in July.

During the summer she felt generally well. She could walk fairly long distances, could climb stairs, and had no trouble eating her meals or in talking. Occasionally she experienced diplopia. In September a duodenal tube was passed again, but this time a stylet was used to avoid any effort of swallowing on her part. No ill effects resulted from this procedure. During the winter the patient remained well for the most part, but on occasions one or other of her symptoms would return for a brief period. From February to May, 1934, she was exceptionally well. She could walk two miles without fatigue, could sew for long periods without any weakness of eyes or hands occurring; she had no trouble in eating or talking. The myasthenic appearance of her face almost entirely disappeared. However, in May she had a recurrence of transitory symptoms such as she experienced during the winter. At this time the glycine was increased to 10 grams three times daily, and the ephedrine reduced to $\frac{1}{8}$ gr. three times a day. Her condition became slightly worse during the next twelve days. Accordingly, the ephedrine was increased to $\frac{1}{4}$ gr. three times daily. This dose of ephedrine in combination with glycine proved the most effective. The patient's condition gradually improved, and, with the exception of the week preceding each menstrual period, during which her symptoms always became much worse, she was able to get about and do things for herself with no marked difficulty in chewing, swallowing or reading. However, she was not able to resume ordinary activity at any time.

In March, 1935, glycine and ephedrine were stopped for four days, with rapid and severe recurrence of all symptoms. When the patient was prostrated, prostigmine, 2.0 c.c., and atropine, 1/100 gr., were given subcutaneously. Rapid and marked improvement in the power and ability to withstand fatigue of all the affected muscles was observed, but she complained of a "tight feeling" in the eyes, nausea and nervousness. The beneficial effect had completely worn off within three hours after the injections, and she felt rather worse than before prostigmine was administered. Subsequently, the patient was given physostigmine salicylate in doses varying from 1/24 to $\frac{1}{8}$ gr., three times daily, with tincture of belladonna in varying doses accompanying each dose of physostigmine. This treatment proved ineffective and her myasthenia

became very severe. On small doses of physostigmine and ephedrine, $\frac{1}{4}$ gr. three times a day, she was a little improved but never so well as when taking only glycine 5 grams and ephedrine $\frac{1}{4}$ gr. three times a day, which was accordingly recommended.

Beginning on July 5, 1935, the patient was given nine daily intramuscular injections of antuitrin, 1 c.c., with no improvement whatever. During August she was taking glycine and ephedrine as formerly prescribed and leading a very restricted life at home. Providing she did not over-exert herself she was moderately comfortable. Commencing on September 23, three days after the onset of menstruation, the patient was given daily subcutaneous injections of prostigmine, 2 c.c., and atropine, gr. 1/150. At this time in the menstrual cycle patient usually feels at her best. Glycine and ephedrine were continued as formerly and she was given sedatives at night to ensure adequate sleep. Six injections were given in all, and following each she experienced a marked beneficial effect which lasted three to five hours, but the increased strength was less marked following the last two injections than it had been after the first four. On September 26 she had to go to bed six hours after the injection because of extreme weakness. On September 27 the weakness, after the effect of the injection wore off, was even more severe and she had great difficulty in walking on the following morning. On September 29 it was decided to discontinue the injections because she was almost unable to stand or use her arms, and the muscles of her eyes and face were very weak; mentally her perceptions were dulled and she complained of difficulty in thinking. The condition of extreme muscular fatigue lasted until October 4 and then gradually over a period of four weeks she regained her former strength while taking glycine, 10 gm., and ephedrine, $\frac{1}{4}$ gr., three times a day. She has continued to take this medication up to the present time and is able to lead a moderately comfortable although restricted life.

The patient's blood pressure readings and heart rate and rhythm, together with the effect of posture, were recorded before and after prostigmine had been administered and showed no essential difference. Repeated blood pressure readings showed the following range: erect, 88/58-80/58; recumbent, 96/66-86/62. The pulse rate always increased in rapidity when the patient assumed the erect posture. The blood pressure findings were interpreted as indicative of postural hypotension. Whether erect or recumbent, examination of the apex beat revealed an irregularity of rhythm characterized by slowing and accelerating, alternatively and irregularly, independent of respiration. Examination of the heart, including an electrocardiographic record, was otherwise negative. The absence of any change in the above findings after prostigmine had been administered suggests that the postural hypotension in this case is independent of the myasthenia gravis.

CASE 2

Mr. D. T., aged 31; occupation, foreman; admitted to Toronto General Hospital July 27, 1931.

History of illness.—Four years previously friends of the patient observed that his right eyelid drooped towards evening. Since that time this had occurred daily although never in the morning. Two years before admission he experienced diplopia for a period of six weeks. This was not constant, but came on after he had been using his eyes for some time and always disappeared with rest. Four months after the diplopia subsided his voice commenced to weaken towards evening, and at this time his speech would sometimes be so indistinct that it was difficult to make himself understood. About the same time difficulty in swallowing food developed half way through each meal. The food became arrested against the roof of his mouth and it was often necessary to use his fingers to push it along. The ptosis, dysarthria and dysphagia continued until the time of admission, becoming increasingly severe, and later were accompanied by a feeling of tiredness in his arms and legs which developed each afternoon during work.

Examination.—A man of fair physique with no muscular wasting. There was a moderate ptosis of the

right upper eyelid, which increased during the examination. The facial muscles were all very weak, giving the face a smooth, ironed-out appearance. He was totally unable to purse his lips for whistling. On showing the teeth or smiling, there was very little retraction of the corners of the mouth. The orbicularis oculorum were so weak that he could offer scarcely any resistance to attempts to open his eyes. Observation of the patient while he was eating showed that after chewing solid food for a few minutes the movements of the jaws became increasingly weaker and required more effort on his part, until chewing ceased altogether. Swallowing, likewise, became increasingly difficult and violent attacks of coughing occurred as a result of food entering the larynx. Occasionally fluids regurgitated through his nose. His speech had a nasal quality constantly, but at the commencement of conversation was clear and intelligible. After giving part of his history the nasal quality increased and syllables became slurred, until finally the words were almost unintelligible. After resting his voice for about half an hour the patient could speak clearly once more. The power in his limbs was good at the beginning of the examination, but repeated movements of any of his limbs against resistance resulted in gradual fatigue from which they recovered after a period of rest. Neurological examination was otherwise negative. Faradic stimulation showed the characteristic fatigue phenomenon in certain muscles of the face and limbs.

Treatment and progress.—The patient was given a course of x-ray irradiation to the thymus gland. A few days after the first treatment improvement was noted, and on discharge from hospital, August 9, 1931, the dysphagia and dysarthria were much less quickly induced and he felt generally stronger in his limbs. The ptosis, however, was unchanged and the facial muscles were still very weak. Improvement gradually continued after discharge so that by October he was able to return to work. At this time there was no tendency to dysphagia or dysarthria, and the ptosis, when present, was very slight. By July, 1932, his facial expression was almost normal. The voice, although slightly nasal, could not be fatigued and his limbs did not tire even after a hard day's work. He continued in good health until January, 1933, when he noted a recurrence of ptosis of his right eyelid towards evening of every day.

Ephedrine, $\frac{1}{4}$ gr. three times daily, failed to benefit him and was discontinued after several weeks. In September, 1933, he tired easily and had difficulty in chewing towards the end of each meal. In December, these symptoms became worse and he suffered from blurring of vision. In January, 1934, walking became difficult because his right leg tired very quickly. Examination on January 15, 1934, showed the patient with his head far back to compensate for a marked ptosis of his right eyelid. No diplopia or strabismus could be demonstrated, but on rapidly moving his eyes a few times an instability of the ocular movements was noted and he complained of objects being blurred. All voluntary and emotional movements of the face were extremely weak. The voice was nasal but could not readily be fatigued. The right hand grip was much weaker than the left, and fingers four and five of the right hand were particularly weak. On testing with repeated movements against resistance the right upper and lower limbs tired in about half the time required to tire the corresponding limbs on the left side.

On February 1, 1934, glycine, 5 grams three times a day, was prescribed. Improvement occurred rapidly and within one week strength had increased in his limbs, blurring of vision had disappeared, as had also the difficulty in chewing and swallowing. The voice became less nasal and developed more cadence. Improvement continued until August, 1934, when he was practically symptom-free. The only physical sign at the present time is a narrowing of the right palpebral aperture due to a slight ptosis which remains constant and does not alter as formerly. The patient is continuing with the glycine treatment and has suffered no recurrence of symptoms up to the present time (April, 1936).

CASE 3

Miss D. B., aged 17, admitted to Toronto General Hospital, June 28, 1932.

History of illness.—In June, 1930, the patient noticed increasing fatigue towards the end of each day. A few months later she experienced diplopia on attempting to read or sew, which disappeared after resting her eyes. At this time she suffered also from difficulty in chewing and swallowing, which developed half way through each meal and increased as she continued eating. Her voice gradually weakened when she conversed for any length of time. These symptoms all became progressively worse, and during the six months previous to admission she experienced a number of terrifying attacks. These occurred independently of any exertion and consisted of severe palpitation, dyspnoea and fear of impending death. Her mother stated that she became very blue during the attacks, but never lost consciousness, and in about fifteen to thirty minutes the symptoms would slowly pass off.

Examination.—Examination showed a poorly nourished young girl, with moderate ptosis of both upper eyelids, and very little play of expression due to severe weakness of the facial muscles. At the commencement of the examination of the eyes there was a slight divergent strabismus present, with some limitation of conjugate movement upwards and to the right. After about five minutes of testing the ocular movements a complete external ophthalmoplegia developed. Following a rest, the ocular movements gradually recovered, although never to a full range of movement. Both emotional and voluntary movements of the facial muscles were very weak and rapidly fatigued with repeated testing. The orbicularis oculorum were so weak that patient could not completely close her eyes. When requested to show her teeth, there was scarcely any retraction of the corners of the mouth, merely a curling of the upper lip. When she attempted to open the lower jaw against resistance the response was very feeble. The voice was high-pitched and weak. When requested to repeat the alphabet she became unable to articulate half way through the fourth repetition, but after ten minutes' rest was able to continue again. The limbs, although generally weak, were not readily fatigued. The gait was not disturbed. Neurological examination, apart from the above findings, revealed no abnormality. Faradic stimulation showed the fatigue phenomenon in the facial muscles characteristic of myasthenia gravis.

Treatment and progress.—The patient was kept in bed at complete rest and given ephedrine, $\frac{1}{2}$ grain three times daily for two weeks. The only improvement noted was in her ability to masticate solid food. She was given a course of x-ray irradiation to the thymus gland, the last treatment on August 6, 1932. From the time of the first treatment progressive improvement was noted, despite the nausea and vomiting which occurred on each occasion. On August 23 she was able to eat well; her voice was much stronger and less easily fatigued; the ptosis was less marked.

A second course of x-ray irradiation was given in September, 1932. Improvement continued, and by October 26, 1932, she felt much stronger and could eat anything without difficulty; her voice did not fatigue with ordinary use; the eyes showed only a slight convergent strabismus even when fatigued but conjugate deviation to the left was incomplete. The ptosis was slight and only occurred late in the day. There had been no recurrence of the attacks with cyanosis and palpitation since admission to hospital.

A further course of x-ray was administered late in November, 1932. Her condition during December showed slight but gradual improvement, although she was still unable to resume ordinary activity. Examination on February 28, 1933, showed that voluntary and emotional movements of the face were all fairly strong; ptosis was absent. She had gained ten pounds in weight in the past four months. The eye movements were full, except for slight weakness of left external rectus, and she experienced diplopia on looking to the left; this became worse after using the eyes, as when walking on busy streets.

Two tablespoonfuls of gelatin, three times daily, were prescribed but during the next three weeks her condition remained essentially unchanged. The gelatin was stopped March 31, 1933, and she was given glycine, 5 grams three times a day. Within a few days the ocular condition improved and she became free of diplopia, only experiencing slight blurring of vision on looking to the left after prolonged use of the eyes. In August, 1933, she was entirely symptom-free and secretly got married. She became pregnant in September, 1933, and during the entire pregnancy felt quite well and had no recurrence of symptoms until April 16, 1934, at which time her sleep was disturbed due to pains associated with the pregnancy. Her expression became slightly myasthenic and diplopia returned on looking to the left. She was admitted to hospital and placed at complete rest in bed until labour commenced.

The glycine was increased to 10 grams three times a day, and sedatives were prescribed at night. Her symptoms cleared up completely after two nights' good sleep. It was found that she was as well on 5 grams of glycine three times a day as on the increased dosage, and the former amount was resumed. On May 6, 1934, the membranes ruptured and she went into labour May 9, at 1.45 a.m. The pains were strong and continued regularly until delivery with low forceps at 7.30 a.m.; the baby weighed seven pounds. Apart from some cyanosis of lips and finger-tips, the patient was in good condition after delivery and showed no myasthenic symptoms. Her pulse rate was 116 per minute four hours after delivery, but gradually became normal in four days. The puerperium was uneventful. She returned home May 22, 1934, and, disregarding advice, soon became pregnant again. She continued taking ephedrine and glycine until April 1, 1935, at which time she stopped it against advice because she felt so well. Her second child was born on May 16, 1935. She suffered no ill effects and has had no recurrence of symptoms. She has taken no medicine of any kind since April 1, 1935, and when last seen in September, 1935, was symptom-free, doing all her own housework and looking after her two children.

CASE 4

R. M., aged 21, a truck-driver, was admitted to Toronto General Hospital, July 20, 1934.

History of illness.—Two years before admission the patient noted a drooping of the left upper eyelid. The ptosis became manifest during the late afternoon of each day and gradually increased until bedtime. The condition completely disappeared after about two weeks and did not recur until three months before admission to hospital. On this occasion, it was accompanied by a similar drooping of the right upper eyelid, and later there was difficulty in rotating the eyes. He complained of a general weakness and rapid fatigue after any exertion.

Examination.—Examination in hospital showed variable ptosis of both eyes, worse towards evening, and greatly improved after rest. An almost complete external ophthalmoplegia was present at times, although, following rest of the eyes, a variable amount of lateral movement of both eyes was usually present, but upward or downward movement was never possible. Marked weakness of both orbicularis oculorum was found on testing. The pupils were moderate in size and reacted well to light and on accommodation. No other abnormalities were found on physical examination. Laboratory investigations, including blood, cerebrospinal fluid and x-ray of skull, were negative.

Treatment and progress.—The patient was given glycine, 10 grams, and ephedrine, $\frac{1}{4}$ gr., three times daily, but at the end of one month no improvement had occurred. The ocular signs showed considerable variation in degree of severity, but no more than before commencing treatment. The glycine and ephedrine were discontinued and the symptoms remained unchanged. On September 12, 1934, glycine, 10 grams three times a day, was recommenced and continued for two weeks with no perceptible effect. On September 26, glycine, 15 grams in saline, was given intravenously and continued once daily until October 13. The patient experienced considerable sub-

jective general improvement in strength, but little objective change was evident. Commencing October 28, 1934, a course of x-ray irradiation to the thymus gland was administered. The patient was discharged from hospital on November 18, 1934, without any definite change having occurred. About the middle of December he commenced to feel better and this improvement gradually continued. He recovered a considerable degree of lateral movement of both eyes and the ptosis was less easily produced and less severe. On April 26, 1935, prostigmine, 2 c.c., and atropine, 1/150 gr., were given subcutaneously. Within thirty minutes ptosis had completely disappeared and power in the orbicularis was much greater. The range of ocular movement increased in all directions, including upwards, but a full range of movement in any direction was not obtained. At the end of two hours the muscles had reverted to their former state. Subsequently no treatment was administered, and in July, 1935, information by letter stated that the patient's ocular movements were continuing to improve gradually. Physostigmine salicylate, gr. $\frac{1}{8}$, and tincture of belladonna, 10 min., twice a day, were prescribed. The patient took this treatment regularly for two weeks but abandoned it because there was no apparent beneficial effect and it made him feel nauseated. Seen in October, 1935, ptosis was still present every afternoon but was not so severe nor so readily produced as formerly. On examination at this time, the only limitation in the range of ocular movements was in conjugate deviation of both eyes to the left and in upward movement of the left eye. Power in the orbicularis oculorum was much improved. Patient stated that he felt stronger generally and that his ocular disability now caused him very little inconvenience.

CASE 5

C. S., aged 29, mechanic, admitted to Toronto General Hospital November 13, 1934.

History of illness.—In 1920 the patient first experienced drooping of the right upper eyelid and diplopia. These symptoms developed towards evening every day and always subsided after rest. Three months after the onset a gradual recovery occurred. In 1927 and again in 1930 the symptoms recurred. On each occasion improvement took place within several months, and during the intervals between relapses he was symptom-free if he did not overstrain his eyes. In 1932 the same symptoms returned more severely than on any previous occasion, and, in addition, his right hand became weak after any strenuous effort. The symptoms persisted and in 1933 the left hand became similarly affected. In May, 1934, the muscles of his jaws tired while eating and swallowing was often difficult. After walking a short distance it became increasingly difficult to raise his feet, and he had several falls going up and down stairs. Both eyelids now tended to droop and diplopia was present most of the time. The symptoms gradually increased so that on admission to hospital he was practically helpless.

Examination.—Examination showed a poorly nourished man with partial ptosis of both upper eyelids, more marked on the right side. The range of movements of the eyes was limited in all directions, but the degree of limitation was to some extent variable, depending on the amount of rest prior to the test. With repeated testing a complete external ophthalmoplegia could be produced. The facial muscles were all extremely weak, particularly the orbicularis oculi. The patient was unable to open the lower jaw against slight resistance. Following a few minutes' conversation, the voice became weak and nasal. The muscles of the trunk were all very weak and he was unable to sit up in bed without using the arms, or to rise to his feet from a recumbent posture on the floor. The upper limbs were weak at all joints, the greatest weakness being in the fingers of both hands. These could not be fully extended or completely flexed voluntarily without a long period of preliminary rest. Power in the lower limbs was less impaired than in the arms. The greatest weakness was in the ankles. After walking a distance or voluntarily flexing and extending the feet at the ankles a number of times a degree of bilateral foot drop would

become apparent, and dorsiflexion of the feet at the ankles would become very weak. Strength in the *museles* gradually returned after a period of rest.

Apart from the above findings, examination was essentially negative. The muscles of the limbs were flahhy hut no localized wasting was present. The tendon reflexes were all present and equal on the two sides and could not be fatigued. The affected muscles showed the fatigue phenomenon characteristic of myasthenia gravis on faradic stimulation.

Treatment and progress.—From November 15 to 29, 1934, glycine, 15 grams in 100 c.c. saline, was administered daily intravenously. On November 17 the patient noted increased power in his legs and freedom from difficulty in chewing or swallowing. Objectively the ptosis was less marked. This improvement was maintained with no change until December 1, two days after discontinuing glycine, when he complained of recurrence of difficulty in chewing and swallowing and that his legs tired more rapidly. The ptosis was more quickly induced. The symptoms gradually increased in severity and on December 5 he was worse than on admission to hospital. On December 7, daily intravenous glycine was resumed, with improvement commencing on the following day. From December 10 to 12 glycine was omitted unknown to the patient and saline alone given intravenously. The symptoms had all recurred by December 12 and the patient suggested that a bad lot of medicine was being used. He stated that a tingling sensation in certain muscles, previously always present following each injection, had not been perceptible after the last three injections. Intravenous glycine was once more resumed and gradual improvement occurred as before. The voice and facial expression also improved on this occasion. Following discontinuance of glycine intravenously the symptoms returned. A few days later glycine, 10 grams three times a day per os, was prescribed. Rapid improvement occurred in the power of the limbs and facial muscles. The ptosis became less frequent and less severe, difficulty in chewing and swallowing disappeared, and the range of ocular movements increased. Within a few minutes of each dose of glycine he experienced a burning, pricking sensation in certain muscles of the face and limbs lasting about twenty minutes. Subsequently ephedrine, $\frac{1}{8}$ gr., was given before each dose of glycine and on this treatment further improvement took place. He became able to fully extend his fingers and to make a complete fist without effort. The ephedrine was increased to $\frac{1}{4}$ gr., three times daily, with steady improvement. A few days later the dose of ephedrine was increased to $\frac{1}{4}$ gr. five times daily, which produced some further improvement in the power of the facial muscles and the muscles of the limbs. Ephedrine, $\frac{1}{4}$ grain, six times daily produced symptoms of intolerance after one week. All treatment was discontinued on March 25, 1935, and the following day the patient became very weak with marked ptosis and ophthalmoplegia, gross weakness of the muscles of the limbs and face, difficulty in chewing and swallowing, and great weakness of the voice. Prostigmine, 2 c.c., and atropine, 1/100 gr., were given subcutaneously on March 26 at 2.30 p.m. Within fifteen minutes power in all the muscles commenced to improve, and at the end of one hour the patient looked and acted like an entirely different man. The power in the muscles of the face and limbs improved greatly and the ptosis disappeared. He was able to walk vigorously, bend over without difficulty, and use his hands in normal fashion, freely and with fair power. Ocular movements showed only a little increased range. There was no difficulty in chewing or swallowing and his voice was clear and strong. By 4.30 p.m. the weakness was returning and at 7.30 his condition was as before the administration of the prostigmine. Glycine, 10 grams three times a day, and ephedrine, $\frac{1}{4}$ grain five times daily, were resumed until April 30, 1935. At this time all other treatment was stopped and patient was given physostigmine salicylate, 1/12 gr., and tincture of helladonna, 10 min., three times daily. His condition became decidedly worse and during two weeks varying doses of physostigmine (gr. 1/6-1/24) were tried hut without benefit. Finally, glycine, 10 grams three times daily, was given as well as physostigmine and helladonna and

the patient's condition improved gradually. On physostigmine, 1/6 gr. twice daily, belladonna, 10 min. twice daily, and glycine, 10 grams three times daily, the power and fatigability of the muscles of the face, trunk and limbs were only a little less satisfactory than when taking glycine and ephedrine as previously.

From August 16 to 24, 1935, inclusive, he received daily intramuscular injections of antuitrin, 1 c.c. This treatment produced no change in his condition during the period of administration or subsequently. On August 28 all other treatment was stopped and he was given prostigmine, 2 c.c., and atropine, 1/150 gr. subcutaneously. Improvement similar to that recorded previously occurred. This treatment was repeated on August 29 and 30. It was then discontinued because the patient received less benefit with each succeeding dose, and the reaction of fatigue which followed the temporary improvement became increasingly severe. On August 31 glycine, 5 grams three times a day, and ephedrine, $\frac{1}{4}$ gr. five times daily, were recommenced and the patient slowly returned to the same condition as prior to the administration of prostigmine. He has remained on this treatment up to the present time (April, 1936) and recent examination showed less fatigue on chewing and swallowing than when he first came to hospital: meals could be eaten in comfort. The ptosis was much less frequent and severe and the range of ocular movements was generally a little increased. The weakness and rapid fatigue of the upper and lower limbs were very marked and confined the patient to a life of invalidism.

CASE 6

Miss G. W., aged 29, typist, admitted to Toronto General Hospital on January 24, 1935.

History of illness.—The patient was perfectly well until four years before admission to hospital. At that time her voice commenced to weaken towards evening each day so that it was an effort to make herself understood. Shortly afterwards she experienced difficulty in swallowing the last few mouthfuls at a meal, and occasionally liquids regurgitated through the nose. Later, fatigue of the jaw muscles developed about half way through each meal and gradually increased effort was required to masticate her food. She continued at work until July, 1932, when she noticed weakness of her arms after any sustained effort. Over a period of a few weeks her upper limbs gradually became more easily fatigued until finally she had to stop work. About this time her eyelids commenced to droop towards evening each day, and it became impossible to open them fully or to close them tightly. During the summer of 1933 the muscles of her neck became weak and her head would frequently fall forward. Her legs tired after walking a short distance and her feet dragged with each step. She had difficulty in stepping on and off street-cars. In June, 1934, her symptoms all became very much worse, and she commenced having blurring of vision almost constantly, and diplopia if she used her eyes very much. The weakness in her limbs was so severe that she was confined to bed. Breathing was frequently a great effort and she often feared impending death from inability to breathe.

Examination.—Examination at this time showed a poorly nourished girl of average intelligence and emotionally stable. There was bilateral partial ptosis and well-marked weakness of all the facial muscles on emotional or voluntary movement. The power of the muscles of the jaw, neck and limbs was much impaired. Her voice was weak and fatigued rapidly when talking, but recovered with rest. There was no gross strabismus at rest, but on repeated testing of ocular movements definite weakness of the internal and external rectus muscles of both eyes could be produced. Examination of the cranial nerves, limbs and trunk was otherwise negative. Various affected muscles showed the fatigue phenomenon characteristic of myasthenia gravis when the faradic current was applied.

Treatment and progress.—The patient was given glycine, 5 grams, and ephedrine, $\frac{1}{4}$ gr., three times a day, commencing June 25, 1934. This treatment was continued until admission to hospital. The day following commencement of treatment she was much improved in

all respects and able to eat her meals in comparative comfort. After six days there was no difficulty in chewing, and no diplopia. She was able to and could use her upper limbs for ordinary tasks. However, the facial muscles, although stronger, were still very weak; the voice was nasal and tired rapidly; and the muscles of her limbs would stand no unusual exertion. This condition remained stationary until admission to hospital on January 24, 1935.

Following admission, ephedrine was discontinued and glycine, 10 grams three times a day, was given alone. Her condition became rapidly worse. Ephedrine, $\frac{1}{4}$ gr. three times a day, produced immediate improvement, and this drug was gradually increased to $\frac{1}{4}$ gr. six times daily, with remarkable improvement, particularly in the power of the limbs. The glycine was discontinued for several days and then recommenced without the slightest effect on her condition.

On March 25 ephedrine was discontinued and during the next two days her condition became alarming. She developed marked weakness of all the muscles of her face, limbs and trunk, attacks of dyspnoea preventing sleep, great difficulty in chewing and swallowing, and her voice was so weak and nasal she could not be understood. On March 28, prostigmine, 2.2 c.c., and atropine 1/100 gr., were injected subcutaneously. Within twenty minutes striking improvement was observed in the power of the muscles of the face and limbs. This continued for one hour, by which time she was able to walk vigorously, step up on a chair with ease, her facial muscles behaved in almost normal fashion, the voice was clear and strong, although still perceptibly nasal. She ate a large meal with no difficulty whatever. Three hours later, however, her condition was the same as before the injection.

During the next four weeks the patient was given physostigmine salicylate in varying doses from 1/24 gr. to 1/6 gr., with tincture of belladonna. She obtained absolutely no benefit from this medication, whether with or without glycine and ephedrine. Even small doses of physostigmine caused her to be nauseated and the symptoms of myasthenia gravis became much worse. Subsequently she was given ephedrine, $\frac{1}{4}$ gr. six times daily, only and has continued on this until the present time (April, 1936) with very satisfactory improvement. The facial expression is only slightly myasthenic; there is no ptosis; retraction of the mouth is good; the forehead can be moderately wrinkled; the weakest muscles are the orbiculares oculorum and complete closure of the eyes is not attained. Chewing and swallowing are well carried out, unless exceptional demands are made. There is no diplopia, no weakness of the neck, and no dyspnoea. The upper limbs do not fatigue in ordinary household work. She can walk moderate distances without fatigue and is gaining weight.

THE RESULTS OBTAINED WITH VARIOUS TREATMENTS EMPLOYED

There is considerable difference of opinion regarding the value of certain methods of treatment advocated for myasthenia gravis. A number of therapeutic measures were used in all the six cases reported above, and an attempt was made to carefully observe the effect of each. It is well recognized that cases of myasthenia gravis are liable to have spontaneous remissions, and that periodic variations in the severity of the symptoms are to be expected, whether treatment is administered or not. This is well shown in the histories of Cases 4 and 5. For these reasons it is often extremely difficult to estimate correctly the value of treatment, and it is necessary to be on guard against drawing false conclusions.

Whenever possible we repeated our observations several times, studying the effect of withdrawal as well as the changes which occurred following the administration of any therapeutic agent. With the exception of Case 4, the patients in this series had severe bulbar symptoms and the urgency of their condition sometimes forced us to employ several remedies in quick succession, rendering correct evaluation difficult.

The results obtained in this small series of cases will be briefly summarized. The methods of treatment used will be considered separately.

*Glycine**.—Glycine per os was given to all 6 patients. The doses varied from 5 to 15 grams three times daily. Symptomatic improvement was observed in 4 patients (cases 1, 2, 3 and 5); no improvement followed the administration of glycine in the remaining 2 patients (cases 4 and 6). Of the patients who benefited, 2 (cases 1 and 5) showed varying degrees of symptomatic improvement within a day or so of commencing treatment, but as quickly returned to their former state whenever the substance was discontinued. However, although definite subjective and objective improvement occurred in these two cases during the administration of glycine, it consisted only in a lessened fatigability of certain affected muscle groups. While the disease was by no means controlled by glycine therapy, these two patients were made more comfortable, and possibly were saved from death by partial relief of their severe bulbar symptoms.

One of the remaining two patients who benefited by glycine (case 3) had already shown marked symptomatic improvement before this treatment was instituted. However, on glycine recovery was much more rapid than previously, and this patient has remained well for two and a half years. That glycine is not essential to maintain this patient free of symptoms is shown by the experience of the past five months, during which time she has taken no treatment and has had no recurrence of symptoms in spite of the strain imposed by childbirth and the entire responsibility of looking after her household.

The remaining patient (case 2) showed more apparent response to glycine than any of the others. His symptoms, which had been progressively increasing for four months, were immediately improved when glycine therapy was commenced. Within five months he became symptom-free. However, this patient recovered from a previous relapse shortly after a course of x-ray treatment to the thymus gland, which would indicate that if glycine had any effect in his recovery it was, at least, not specific.

Dosage was not an important factor in the cases which received glycine. Cases which were symptomatically improved by 5 grams three times daily did not receive greater benefit by increasing the dose. Glycine, 15 grams in 100 c.c. of saline, was administered intravenously daily for a period of several weeks to 2 patients (cases 4 and 5). One (case 5), who also showed some improvement on glycine per os, was apparently helped by intravenous glycine although the effect was not so great as with glycine per os. That the intravenous glycine was of some benefit was indicated by the relapse which occurred when glycine was omitted from the intravenous without the patient's knowledge. The other patient (case 4) who received glycine intravenously showed no objective improvement. This patient also failed to respond to glycine per os.

Ephedrine—Ephedrine was administered to all the patients, but had no effect in relieving the symptoms in numbers 2, 3 and 4. The remaining three (cases 1, 5 and 6) experienced symptomatic improvement while taking the drug, but in only one (case 6) was the action apparently

*We are indebted to the Connaught Laboratories for the supply of glycine used in this investigation, which was provided through the kindness of Dr. E. W. McHenry.

specific. It was clearly shown by repeated observations that ephedrine alleviated the severe symptoms in this case, and that withdrawal of the drug resulted in a rapid relapse into a state of profound myasthenia. It may be of significance that this patient obtained maximum benefit from an amount of ephedrine ($1\frac{1}{2}$ gr. daily) which was not tolerated in other cases.

The other two patients (cases 1 and 5) obtained much less benefit from ephedrine alone. Some symptomatic improvement was noted, but no definite alleviation of symptoms was evident. Both these patients, unlike number 6, also received benefit from glycine, but showed maximal improvement when they were receiving both glycine and ephedrine. In both instances the best results were obtained by pushing the drug to the limits of tolerance. This contrasts with glycine therapy, in which larger doses appear to be no more beneficial than small ones.

X-ray irradiation of the thymus gland.—This method of treatment has been known for many years, but, despite encouraging reports of individual cases benefited by the treatment, it does not seem to have been used very extensively. In our small series of cases the results would appear to indicate that it has definite value in bringing about a remission. A course of treatment consisted of three irradiations with a dosage of 800 R. units each. These were applied to the mediastinum in the anterior, right and left posterior oblique positions.

Four patients were treated by this method (cases 1, 2, 3 and 4). In none of them was any enlargement of the thymus gland demonstrated clinically or by x-ray. Two showed marked improvement within a short time of receiving a course of treatment. Patient 3, with a two-year progressive history of symptoms, commenced to improve a few weeks after the first treatment and proceeded gradually to a complete remission. Patient 2, with a four-year history of myasthenic symptoms, commenced improving a few days after the last treatment and became symptom-free in two months. The remission in this case lasted two years before recurrence of symptoms. This second relapse was treated with glycine with equal success. In the other two cases treated by x-ray it is doubtful what part the treatment played in the improvement. Case 1 failed to show definite improvement until three months following the last treatment. At that time only a partial relief from symptoms occurred, which lasted six months. The progressive increase in symptoms over a period of three years prior to the administration of x-ray therapy is the only reason for assuming that the treatment may have been responsible for the improvement.

In Case 4 there had been a previous relapse of two weeks' duration from which spontaneous recovery occurred. Prior to receiving x-ray treatment symptoms had been present for six months. Improvement commenced six weeks after the last treatment and during the past nine months has slowly continued. The same doubt regarding the importance of x-ray therapy in effecting this improvement exists as in Case 1. In Cases 2 and 3 it seems probable that the remissions may have been started by this method of therapy. Despite the absence of any conclusive evidence, one feels that this treatment should be used more extensively than it has been in the past.

Prostigmine.—The four patients (cases 1, 4, 5 and 6) having symptoms of myasthenia gravis at the time the action of this drug was reported were each given an injection of prostigmine, 2.2 c.c., and atropine, 1/150 gr., subcutaneously. A marked temporary improvement in the power and resistance to fatigue of the affected muscles was noted in all cases. The improvement developed rapidly, reaching its maximum within an hour following the injections. However, the muscles gradually resumed their former state in a few hours and the myasthenic symptoms became usually slightly worse than they had been before the treatment was administered. On this dosage of prostigmine complete relief of symptoms was not obtained in any case. The muscles which were least benefited were those which had been weak for the longest time. Two patients (cases 1 and 5) received prostigmine on successive days. The beneficial effects were a little less marked with each succeeding injection, and the weakness and fatigability of the affected muscles became pro-

gressively worse after the effect of the drug had worn off, so that on the seventh and third days, respectively, it was considered unsafe to give any further injections to these patients.

Physostigmine salicylate.—Physostigmine salicylate, in doses varying from 1/24 gr. to 1/6 gr., with tincture of belladonna, 5 min. to 15 min., was administered to four patients (cases 1, 4, 5 and 6) without any beneficial effect. In all cases myasthenic symptoms actually became worse during the treatment and were usually associated with varying degrees of nausea and malaise. When glycine or ephedrine were substituted for physostigmine a rapid return to their former condition was noted in patients 1 and 6, suggesting that their relapses had been due to stopping these substances. One patient (case 5) showed definite improvement when glycine, 10 grams three times a day, was added to the treatment of physostigmine salicylate, 1/6 gr., and belladonna, 10 min., twice daily. However, this patient, unlike the others, had suffered no nausea or general symptoms as a result of the physostigmine.

Antuitrin.—Two patients (cases 1 and 5) received nine consecutive daily injections of 1 c.c. antuitrin intramuscularly. In neither case was any benefit obtained.

DISCUSSION

Judging by the experience in this series of cases, the prognosis for life in myasthenia gravis would appear good when modern methods of treatment are employed. With the exception of Case 4 all the patients in this series were severely prostrated at some period of their illness, yet no fatalities have occurred to date. On the other hand, only 2 of the 6 patients have recovered sufficiently to permit return to full activity. Of the remaining patients, two are able to lead restricted lives with moderate comfort, but would only be capable of part-time duty. The other two are unable to do work of any kind.

In this small group of cases the results of treatment clearly indicate that great variation exists in the response of patients to the various remedies. This would suggest that the factors which determine the development of the symptom-complex known as myasthenia gravis may vary in different individuals. With the exception of antuitrin intramuscularly and physostigmine salicylate per os, which produced no definite improvement in the patients to whom they were administered, all the other forms of therapy were beneficial in certain cases. Of these latter, prostigmine subcutaneously gave the most consistent results, but the temporary nature of the improvement, the method of administration, and the cost all render it impracticable for continuous use. Further, it must be considered that the disturbed function of the muscles is not fundamentally altered by the administration of prostigmine. This is shown by the complete reversion of the affected muscles to their former state when the effect of the drug wears off. It has been suggested that the increased usage of

the muscles permitted during the temporary remissions may prove actually harmful if repeated too often. This was shown in two of our patients (cases 1 and 5) with severe generalized myasthenia. Daily administration of prostigmine had to be discontinued because of very pronounced weakness which developed five hours after the sixth injection in one case, and about the same time after the third injection in the other. It would seem that prostigmine subcutaneously is not likely to prove of much value in the therapy of this disease apart from its uses as an emergency measure in treatment and as a therapeutic test in diagnosis.

There still remain at our disposal three principal forms of therapy which appear to be of value in this disease; x-ray irradiation of the thymus gland, glycine, and ephedrine. The first of these may be effective in bringing about a remission. The latter two remedies, either together or separately, may give some measure of symptomatic relief. To decide which treatment will give the best results requires a process of trial and error. In evaluating the results of any remedy it is necessary to consider the tendency of the disease to spontaneous remissions and the frequent variation in the severity of the symptoms which may occur as a result of many factors, both intrinsic and extrinsic.

It was observed repeatedly in these patients that minor infections, emotional stress, hot baths, and mild gastrointestinal upsets were liable to produce marked increase in the fatigability and weakness of the affected muscles. In certain female patients a relapse is associated with each menstrual period (See case 1), whereas in other patients the severity of the symptoms bears no relation to the menstrual cycle (cases 3 and 6). Likewise, as pointed out by Laurent,¹² pregnancy in some patients may bring about a relapse, whereas in others a remission occurs while the patient is pregnant. In this connection, it is of interest that patient No. 3 has had two pregnancies in the past two years without a return of symptoms. There can be no doubt that exercise to the extent of fatigue aggravates the disease, particularly if continued over many days or weeks. These patients are always benefited by rest such as is obtained when they stop work. However, it is questionable whether complete rest in bed for long periods is of much value. In our experience, patients usually do better if they are allowed to take mild exercise short of fatigue.

SUMMARY AND CONCLUSIONS

1. Six cases of myasthenia gravis are reported, and their responses to different types of treatment are discussed in some detail.

2. Allowing for the tendency of the disease to spontaneous remissions and the frequent variation in the severity of the symptoms in the absence of treatment, the results in this series tend to confirm the view that x-ray irradiation of the thymus gland may be effective in some cases in bringing about a remission of months' or years' duration, and that glycine and ephedrine, either together or separately, are of value in obtaining symptomatic improvement in certain cases.

3. Glycine intravenously may produce symptomatic improvement in patients who respond to glycine per os, but it is apparently less effective. However, it might be useful as an emergency measure when a patient is unable to swallow.

4. The variability noted in the response of different patients to different remedies, particularly to glycine and ephedrine, is emphasized, and this suggests that the clinical syndrome of myasthenia gravis may be caused by different chemical factors.

5. Two methods of treatment which have been advocated failed to give any beneficial results in our experience, namely, physostigmine salicylate per os and antuitrin intramuscularly.

6. The dramatic effect of prostigmine, administered subcutaneously, in producing a temporary improvement was observed in four cases, but it is impracticable for continued use, and the fatigue subsequent to several consecutive injections may reach serious proportions.

7. The prognosis for life is good with modern methods of treatment, but it is only fair for complete remission of symptoms. Two of the cases in this series are in remission and the patients are carrying on at their regular activities. Two have improved to a degree where part-time occupation is possible. The remaining two patients, although somewhat improved by treatment, are totally incapacitated for any form of remunerative occupation.

I wish to express my thanks to Prof. Duncan Graham for permission to publish these case reports.

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THE RADIOLOGICAL TREATMENT OF CANCER: METHODS AND RESULTS 1928 - 1935

II. CARCINOMA CERVICIS UTERI*

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FOR the past seven years an organized group representing the Departments of Gynaecology and of Radiology in the Toronto General Hospital has undertaken the joint study and treatment of a steadily increasing number of patients suffering from carcinoma of the uterine cervix. Following the organization of the Ontario Institute of Radiotherapy in 1934 the work has been carried on by the same group, thus enabling a report to be presented covering the entire period 1928 - 1935. During that time 227 public ward patients were treated with radium supplemented by high voltage x-ray. This series includes only those cases which had not received any active treatment previously, nor does it include cases in which the tumour involved the stump of cervix remaining after supra-vaginal hysterectomy performed at some previous date for a non-malignant condition. The comparatively small number of cases treated does not present a logical basis upon which to state percentage of cure rates. Nevertheless the follow-up has been very satisfactory, due in no small part to efficient social service and secretarial work.

STATISTICAL TABLES

The Tables which follow present the survival of patients after treatment. Therefore the fact that three patients are reported as dying from extraneous disease does not affect the percentage survival rate, as they have been included in the report notwithstanding the fact that one died from tuberculosis and another from diabetes, although being apparently free from cancer. The other patient died from pulmonary embolism four days after treatment and has been specially noted, to draw attention to this one operative death.

Table I presents the survival Table of the whole series. The two five-year groups are very small. It is felt, however, that the one- and two-year survival groups present an interesting comparison, as the improvement under more complete and standardized treatment is evident. The analysis at the foot of the Table suggests that it may be anticipated that these same good results should carry through to the five-year period. At any rate the five-year period is no longer taken as the absolute criterion of cure, but has become rather a figure of speech. Over 40 per cent of the patients have been over fifty

* The first article of this series appears in the September issue of this Journal.

years of age, and for them at least the mark of success may well be a symptom-free year.

CLINICAL CLASSIFICATION

The classification of Schmitz has been followed. The individual factor markedly affects any tabulations, and it is only after repeated examinations, vaginal, rectal and by speculum, that an accurate estimate of the extent of the disease may be determined. All extensive growths have an associated inflammatory reaction which not infrequently causes considerable cellulitis. In treated cases there often is scar-tissue formation in the recto-vaginal septum which may be very hard to differentiate except by repeated observations.

The extent of the disease is the basis for prognosis. Early diagnosis remains very difficult, as cancer of the cervix in its early phase is as silent as early malignant disease elsewhere. The symptoms commonly associated with its further development often cause the patient no alarm, or else fear keeps her from consulting a physician. The pitfalls which face the physician are many. Experience shows that a quarter of our patients have been under forty years of age and in many cases, in the absence of careful examination, the incipient growth had been treated by drugs, douches and local applications. Stage I carcinoma is rarely marked by well established symptoms, and must be diagnosed, often on a mere suspicion, by biopsy or diagnostic curettage.

It has been stated that post-operative cases have not been included in this review. The fact seems to be hard to establish that the eradication of cancer of the cervix by hysterectomy is an extremely difficult procedure, even in the hands of the most skilled, and yet a considerable number of patients have come to the Institute a few weeks after hysterectomy with the pelvis already filled by malignant involvement of the vaginal vault and cellular tissues. In several cases the cervix was *in situ* and the body of the uterus alone had been removed. The Tables show that there has been an increasing percentage of early cases coming to the clinic, and it is to be noted that when this was not the case, as in 1932, when only 40 per cent were stage I and II, as compared to 54 per cent in 1933, the results of treatment reflected this fact. Naturally, the main problem is the control of cancer, once invasion of the surrounding tissues has developed.

It is probable that the failure to cure many early cases is due to inability to determine the lymphatic spread. The value of high voltage x-ray as a supplement to radium is evident in the results from 1931 on to the present, and it was only last year (1935) that the fractionated method of Contard was adopted as a routine. The results for that year speak for themselves, especially in advanced cancer, where often it was the only form of treatment. These years of observation have taught that the time is gone when a cure may be expected by a day or two of treatment. Just as the patient suffering from tuberculosis must face with forti-

TABLE I.

CARCINOMA OF CERVIX UTERI: SURVIVAL TABLE BY YEARS CONTROLLED TO DECEMBER, 1935

GENERAL TABLE INCLUDING ALL CASES IN THIS REPORT: PERIOD 1929 TO 1935, INCLUSIVE

Year	Total	1 Yr.	Per-centage	2 Yrs.	Per-centage	5 Yrs.	Per-centage
1929	11	5	45.4	3	27.1	3	27.1
1930	18	10	55.5	7	38.8	5	27.7
1931	30	19	63.3	16	53.3		
1932	30	16	53.3	10	33.3		
1933	37	24	66.6	22	61.1		
1934	47	29	61.7				
1935	54	43	79.6				
Total	227						

Total of 227 cases of carcinoma cervix uteri were treated during the period 1929 to 1935.

Of these 134 are living and 104 are dead or untraced.

Of the 104 dead or untraced:

99 have died of cancer.

3 have died of extraneous disease.*

2 are untraced.

Of the 123 living:

3 are living 6 yrs. of whom 3 are symptom-free.**

5 are living 5 yrs. of whom 5 are symptom-free.

13 are living 4 yrs. of whom 13 are symptom-free.

8 are living 3 yrs. of whom 8 are symptom-free.

22 are living 2 yrs. of whom 19 are symptom-free; 3 are still under treatment.

29 are living 1 yr. of whom 23 are symptom-free; 6 are still under treatment.

80 are living 1 to 6 yrs. of whom 71 are symptom-free; 9 are still under treatment.

43 are living less than 1 yr. of whom 18 are symptom-free; 25 are still under treatment.

123 living December, 1935, of whom 89 are symptom-free; 34 are still under treatment.

Percentage of cases untraced, approximately 0.89%.

*One of these patients died of pulmonary embolism four days after radium treatment.

**The term symptom-free throughout this report is used to indicate that the patient is free from any evidence of the malignant disease for which treatment was undertaken as determined by the usual methods of clinical investigation.

tude months and years of care and supervision, so must the cancer patient. The concentration of a group of patients so controlled permits constant rechecking of results and so the evolution of more rational and thorough treatment.

RADIOLOGICAL METHODS

The analysis of the results of treatment as indicated in the Tables accompanying this paper was originally undertaken for the purpose of discovering to what extent the methods used in treatment might be considered satisfactory or if changes might be required. The conclusions reached may be indicated briefly, though space does not permit descriptions of technical procedures.

Stage I.—There were 34 cases altogether, of whom one patient was untraced and one had died of tuberculosis four years after treatment of her cancer without recurrence of the growth. There had been no deaths from cancer in this group in the 7-year period and of 32 living pa-

TABLE II.

CARCINOMA OF CERVIX UTERI: STAGE I
SURVIVAL TABLE BY YEARS
CONTROLLED TO DECEMBER, 1935

Key: D.D.—Died of disease, i.e., cancer.
D.E.D.—Died of extraneous disease.
Unt.—Untraced.

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	1	1	1	1	1	1	1
1930	3	2	2	2	2	2	
		1 unt.					
1931	5	5	5	5	4		
					1 D.E.D.		
1932	1	1	1	1			
1933	7	7	7				
1934	11	11					
1935	6	6					
Total	34						

Total of 34 cases of carcinoma of cervix uteri, stage I, were treated during the period 1929 to 1935. Of these 32 are living and 2 are dead or untraced December, 1935.

Of the 2 dead or untraced:

1 has died of extraneous disease (tuberculosis).
1 is untraced.

Of the 32 living:

1 is living 6 yrs. of whom 1 is symptom free.
2 are living 5 yrs. of whom 2 are symptom-free.
4 are living 4 yrs. of whom 4 are symptom-free.
1 are living 3 yrs. of whom 1 is symptom-free.
7 are living 2 yrs. of whom 7 are symptom-free.
11 are living 1 yr. of whom 11 are symptom-free.

26 living 1 to 6 yrs. of whom 26 are symptom-free.

6 living less than 1 yr. of whom 4 are symptom-free;
2 are still under treatment.

32 living December, 1935; of whom 30 are symptom-free; 2 are still under treatment.

tients 30 were symptom-free. The two patients who could not be so considered had been treated within the year.

It was felt that the results in this group were very encouraging, and accordingly no drastic changes have been made in method. Patients in this group are treated primarily by radium. The dose used is 8,400 mg. hrs., using a filter equivalent to 1.5 mm. of platinum within the uterus and 2.5 mm. in the vaginal portion of the applicator. The chief point in carrying out the treatment is meticulous care in placing the radium, combined with the least possible handling and traumatism of the tissues.

TABLE III.

CARCINOMA OF CERVIX UTERI: STAGE II.
SURVIVAL TABLE BY YEARS
CONTROLLED TO DECEMBER, 1935

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	4	3	1	1	1	1	1
		1 D.D.	2 D.D.				
1930	7	5	3	3	2	2	
		2 D.D.	2 D.D.		1 D.D.		
1931	10	7	6	6	6		
		2 D.D.	1 D.E.D.				
		1 unt.					
1932	11	11	8	6			
			3 D.D.	2 D.D.			
1933	13	12	10				
		1 D.D.	2 D.D.				
1934	19	12					
		7 D.D.					
1935	18	18					
Total	82						

Total of 82 cases of carcinoma cervix uteri, stage II, were treated during the period 1929 to 1935. Of these 55 are living and 27 are dead or untraced December, 1935.

Of the 27 dead or untraced:

25 have died of cancer.

1 has died of extraneous disease (diabetes).
1 is untraced.

Of the 55 living:

1 are living 6 yrs. of whom 1 is symptom-free.
2 are living 5 yrs. of whom 2 are symptom-free.
6 are living 4 yrs. of whom 6 are symptom-free.
6 are living 3 yrs. of whom 6 are symptom-free.
10 are living 2 yrs. of whom 9 are symptom-free.
10 are living 2 yrs. of whom 9 are symptom-free;
1 is still under treatment.
12 are living 1 yr. of whom 9 are symptom-free;
3 are still under treatment.

37 living 1 to 6 yrs. of whom 33 are symptom-free;
4 are still under treatment.

18 living less than 1 yr. of whom 11 are symptom-free;
7 are still under treatment.

Total of 55 living December, 1935, of whom 44 are symptom-free; 11 are still under treatment.

Stage II.—There were 82 cases in this group. Fifty-five are living while 26 are dead and 1 is untraced. Of the 55 living patients 44 are

symptom-free and 11 are still under treatment or are not free of disease. It is our conclusion that only the early cases in this group are suitable for radium as the primary method and that all the late stage II cases should be treated as recommended for the next group. The technical details of the radium treatment are much as for stage I.

Stage III.—The study of the results in this group was most instructive. Prior to the extended use of high voltage x-ray therapy, as will be seen by a reference to Table IV, the deaths in each year in the stage III cases were usually more than 50 per cent. This was accompanied by great difficulty in treatment, owing to massive tumours, secondary infection, etc., and the chief effort in treatment was to perfect ways and

TABLE IV.

CARCINOMA OF CERVIX UTERI: STAGE III.
SURVIVAL TABLE BY YEARS
CONTROLLED TO DECEMBER, 1935

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	6	1 5 D.D.	1	1	1	1	1
1930	5	2 3 D.D.	2	2	1 1 D.D.	1	
1931	9	7 2 D.D.	5 2 D.D.	3 2 D.D.	3		
1932	11	4 7 D.D.	1 3 D.D.	1			
1933	9	4 4 D.D. 1 D.E.D.	4				
1934	10	5 5 D.D.					
1935	19	14 5 D.D.					
Total	69						

Total of 69 of cases of carcinoma of cervix uteri, stage III, were treated during the period 1929 to 1935. Of these 29 are living and 40 are dead, December, 1935.

Of the 40 dead:

39 have died of cancer.

1 has died of extraneous disease (post-operative embolism)

Of the 29 living:

1 is living 6 yrs. of whom 1 is symptom-free.

1 is living 5 yrs. of whom 1 is symptom-free.

3 are living 4 yrs. of whom 3 are symptom-free.

1 is living 3 yrs. of whom 1 is symptom-free.

4 are living 2 yrs. of whom 3 are symptom-free;

1 is still under treatment.

5 are living 1 yr. of whom 3 are symptom-free;

2 are still under treatment.

15 living 1 to 6 yrs. of whom 12 are symptom-free;
3 are still under treatment.

14 living less than 1 yr. of whom 3 are symptom-free;
11 are still under treatment.

Total of 29 living December, 1935, of whom 15 are symptom-free; 14 are still under treatment.

means of dealing with this. Following the more thorough application of high voltage x-ray therapy (200 K.V.P.) there has been a decided improvement. In cases which respond favourably the massive tumours undergo recession, secondary infection disappears, ulceration heals, and the technique of the radium application is greatly simplified. Hence in all stage III cases treatment is commenced by a very thorough and protracted course with high voltage x-ray. It is very probable that *all* stage II cases and certainly *all late* cases in that group would be greatly benefited by being treated in a similar manner. The chief difficulties in carrying out such a procedure are economic and technical. Each treatment occupies from forty to sixty minutes, and in patients weighing more than 150 lbs. two such treatments per day are desirable. Such daily treatments (except Sunday) are continued for from four to six weeks. Following the completion of the x-ray series the radium treatment is carried out either immediately or after a short interval, depending upon the individual case. Comparing the figures for the year 1932 with those for 1935, there has been an improvement of about 26 per cent, almost all of which is due to the more thorough application of this method. To what extent this apparent improvement will influence future figures cannot of course be predicted, though it seems reasonable to expect a substantial increase in the percentage cure rate. If this should prove to be the case it will have a very important bearing on the manner of dealing with this disease. Technical methods in carrying it out permit of much greater refinement, which should add still further to benefits already obvious. For the present therefore the conclusion reached is that in all stage III cases and in some at least of stage II the primary method of treatment should be by the protracted fractional method of administering high voltage x-ray therapy and that this should as a rule precede rather than follow the use of radium.

Stage IV.—In common with others we have reached the conclusion that radium is seldom if ever indicated as the primary method of treatment during this stage. Accordingly treatment is commenced by high voltage x-ray and radium is used only in those few cases whose progress under this form of therapy reaches a point where its use is indicated. Cures are not expected, but

much palliation may sometimes be obtained as indicated by prolongation of life, and, perhaps

TABLE V.

CARCINOMA OF CERVIX UTERI: STAGE IV.
SURVIVAL TABLE BY YEARS
CONTROLLED TO DECEMBER, 1935

Year	No.	1 Yr.	2 Yrs.	3 Yrs.
1930	3	1 2 D.D.	— 1 D.D.	
1931	6	— 6 D.D.		
1932	7	— 7 D.D.		
1933	8	1 7 D.D.	1	
1934	7	1 6 D.D.		
1935	11	5 6 D.D.		
Total..	42			

Total of 42 cases of carcinoma of cervix uteri, stage IV, were treated during the period 1929 to 1935. Of these 7 are living and 35 are dead, December, 1935.

Of the 35 dead:

35 have died of cancer.

Of the 7 living:

1 is living 2 yrs. and is still under treatment.

1 is living 1 yr. and is still under treatment.

5 are living less than 1 yr. and are still under treatment.

Total of 7 living December, 1935; of whom 7 are still under treatment.

more important than this, the added comfort which is derived from cessation of foul discharge and relief of pain. Even this is not constant and therefore every effort should be made by means of early diagnosis and prompt and efficient treatment to permit as few cases as possible to reach this stage. We know of no more effective way of adding emphasis to this observation than by inviting a comparison of the results of treatment in groups I and IV as recorded in the Tables which accompany this paper. It is scarcely necessary to draw attention to the obvious fact that all the cases in group IV were at one time in stage I, and had they been recognized and promptly treated at that period the prognosis for each would have been as favourable as it now is hopeless.

One of the greatest contributions which the medical profession can make towards this end would be to refer such cases as are being sent for treatment with as little preliminary interference as possible, except possibly a biopsy. Partial operations are worse than none at all and seriously jeopardize the prospect of successful radiotherapy. Since the latter clearly offers the patient more hope of cure than any other method at present available it should be carried out under as favourable conditions as possible.

THE RADIOLOGICAL TREATMENT OF CANCER: METHODS AND RESULTS

1928-1935

III. MALIGNANT LESIONS OF THE TONSIL AND ITS PILLS

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THE clinical material upon which this study is based consists of 52 cases of malignant lesions involving the tonsil or its pillars, treated during the period 1928-1935, inclusive. Of these, 42 cases were carcinomata while 10 were sarcomata. Of the 42 patients diagnosed as having carcinoma 17 are living, of whom 15 are symptom-free*; 2 have died of extraneous dis-

ease without recurrence of their malignant growth which had been controlled by treatment; 21 have died of cancer; and 2 are untraced. Of the 10 sarcoma patients, 5 are living and 5 are dead. The details in each group are as follows:

CARCINOMA OF THE TONSIL

A total of 42 cases were treated during the period 1928 to 1935. Of these 17 are living and 25 are dead or untraced, December, 1935.

Of the 25 dead or untraced:

21 have died of cancer.

3 have died of extraneous disease.

1 is untraced.

* The term "symptom-free" is here used to indicate that the patient is free from any evidence of the malignant disease for which treatment was undertaken, as determined by the usual methods of clinical investigation.

Of the 17 living:

2 are living 7 yrs. of whom 2 are symptom-free.
 1 is living 6 yrs. of whom 1 is symptom-free.
 2 are living 3 yrs. of whom 2 are symptom-free.
 2 are living 2 yrs. of whom 2 are symptom-free.
 3 are living 1 yr. of whom 2 are symptom-free.

10 living 1 to 7 yrs. of whom 9 are symptom-free.
 7 living 1 yr. or less of whom 6 are symptom-free.

Total of 17 living, December, 1935—40%

Of these 15 are symptom-free—35%

2 are still under observation.

SARCOMA OF TONSIL

Ten cases of sarcoma of tonsil were treated during the period 1928 to 1935. Of these 5 are living and 5 are dead.

Of the 5 dead:

All have died of sarcoma.

Of the 5 living:

1 has survived 6 yrs. and is symptom-free.
 1 has survived 3 yrs. and is symptom-free.
 1 has survived 2 yrs. and is symptom-free.
 2 are living 1 yr. or less.

Total of 5 living December, 1935; of whom all are symptom-free. (All were lympho-sarcomata.)

All cases accounted for.

PATHOLOGY

The pathological classification has been simplified as much as possible, and according to this nomenclature the tumours fell into the following groups:

TABLE I.

Epidermoid carcinoma.....	28
Transitional cell carcinoma.....	5
Basal-cell carcinoma.....	2
Carcinoma, not specified.....	3
Lympho-sarcoma.....	5
Fibro-sarcoma.....	2
Hodgkin's sarcoma.....	1
Sarcoma, not specified.....	2
	—
	48
Biopsy negative.....	1
No biopsy recorded.....	3
	—
	52

The patient in whom the biopsy was negative died within six months of cancer of the tonsil. Of those in whom no satisfactory biopsy was recorded, one was case No. 30-2, clinically very advanced, and is one of the untraced cases. A second was case No. 31-1, also advanced, and this patient died of mediastinal involvement two years after the treatment of his primary lesion. The third was case No. 29-2 who is still alive and symptom-free. His was a very typical case on clinical examination, and the diagnosis is undoubtedly accurate.

Table II shows the cases re-grouped according to the pathological findings and indicates the ultimate result in each group.

TABLE II.

	Total Cases	Living	Dead	Untraced
Epidermoid carcinoma.....	28	10	17	1
Transitional cell carcinoma.....	5	3	2	
Basal-cell carcinoma.....	2	2	0	
Carcinoma, not specified....	3	1	2	
Lympho-sarcoma.....	5	5	0	
Fibro sarcoma.....	2	..	2	
Hodgkin's sarcoma.....	1	..	1	
Sarcoma, not specified.....	2	..	2	
Negative biopsy.....	1	..	1	
No biopsy.....	3	1	1	1
	52	22	28	2

Considering the question of success or failure therefore from the standpoint of the pathological findings alone, it would appear that the opinion generally held is correct, namely, that of the carcinomata the basal-cell type offers the most favourable prognosis, the transitional type the next most favourable, and the epidermoid type is the least favourable as well as the most common lesion.

In the sarcomata it will be noted that all the successful results were in the group of lympho-sarcomata, in which in fact there were no failures. While the number of cases is too small to give this observation a great deal of significance it does serve to emphasize the radio-sensitiveness of this type of tumour.

ANALYSIS OF RESULTS

Apart from reasons inherent in the pathological nature of the tumours themselves, success or failure may be influenced by a number of complex factors, such as the age of the patient, his general condition and willingness to co-operate, the duration and extent of the growth, etc. But, broadly, medical interest is centred on two questions mainly: to what extent was treatment successful in controlling (1) the primary lesion and (2) glandular secondaries, and in each case what part did radiotherapy play and what part was taken by surgery? To go into great detail in answering these questions is outside the scope of the present paper but much of the essential information may be condensed and is as follows:

TREATMENT OF THE PRIMARY LESION

The carcinoma group—42 cases.—In 39 of these radiotherapy was the sole method used in dealing with the primary lesion. Disappearance of the lesion and primary healing were obtained

in 32, while in 3 no opportunity of re-examination following treatment was afforded, so that accurate information on this point was not obtainable. In the remaining 4 cases the treatment failed to produce satisfactory healing. Chief interest therefore attaches to the 32 cases in which healing of the primary lesion was obtained. Of these 21 have remained healed without recurrence. Two additional cases healed and remained healed without recurrence until death ensued from other causes. Two others healed, then recurred locally, were again treated, and healed without subsequent recurrence. Thus in 25 of this group of 33 cases the primary lesion may be said to have been successfully controlled by radiotherapy. The other three cases of the series had previously been treated by surgical excision and were referred for post-operative prophylactic treatment. This was ineffective, as all three developed recurrences, either locally or elsewhere, and died of the disease. One of these patients might possibly have been saved by a surgical dissection of glandular secondaries but refused. It is our feeling that in this field if patients are to be referred for radiotherapy better results may be expected if no preliminary operation is undertaken, except in those cases in which the diagnosis has resulted from examination of material removed during simple tonsillectomy.

The sarcoma group—10 cases.—In two of these previous tonsillectomies had been performed and upon a study of the material removed the diagnosis had been made. In one case the disease involved both tonsils, and slides from both were positive. In this case recurrences were already present when treatment was undertaken, together with massive involvement of regional glands.

Of the 10 cases immediate healing of the primary lesion by radiotherapy was obtained in 8, one was treated post-operatively without the presence of a primary, and the tenth was a young child having an enormous primary in whom no satisfactory treatment was possible. None of the 9 cases in whom the primary lesion was controlled developed local recurrences, death being due in those cases whose treatment was finally unsuccessful to other factors (remote metastases 3 cases, failure to control glands, 1 case).

THE TREATMENT OF GLANDULAR SECONDARIES

This is a more complex problem. Of the 42 cases of carcinoma 14 presented no evidence of glandular secondaries on admission. In 11 of these no glands ever developed while three developed glandular secondaries at a later date. Twenty-eight patients had enlarged glands on admission. These were classified in three categories: (a) small, discrete glands, few in number, operable, 11 cases; (b) numerous, larger but not matted, operable, 12 cases; (c) massive involvement, inoperable, 5 cases; total 28 cases. One of the latter also presented extensive involvement of the mandible. All of the last group would be regarded as hopeless cases, and treatment was undertaken largely as a palliative measure.

The principle underlying the treatment of glandular secondaries in dealing with the cases here reported has been to operate upon all cases considered operable by the surgical consultant, but where possible this procedure has been postponed until after the treatment of the primary lesion has been completed, since, unless this lesion can be successfully controlled by radiotherapy, the patient should not be submitted to a major surgical procedure. This interval also provides an opportunity of carrying out a course of pre-operative irradiation of the glandular areas. If the glands disappear following this radiotherapy no operative procedure is undertaken, and "routine" dissections of the neck in the absence of palpable glandular involvement have not been done. The whole question of what is considered the proper method of dealing with the problem of glands will be more fully discussed in a later paper. For the present the facts are as follows.

1. *Cases without glandular involvement on admission*.—As has previously been stated there were 14 such cases and of these only 3 later developed glands. The extent to which this affects the final outcome is instructive. Of the 11 in whom no glands ever developed 6 are living and symptom-free; 2 additional patients died of intercurrent disease without recurrence, making 8 of the 11 cases which may be considered as having had a successful result from treatment, a much higher percentage than in the group having glandular complications as will be seen presently.

Cases in whom no glands developed—11.

Living and symptom-free—6.

- 1 has survived 7 years.
- 1 has survived 6 years.
- 2 have survived 2 years.
- 2 have survived 18 months.

Cases who have died—5.

Cases who have died of intercurrent disease—2.

- 1 pneumonia, without recurrence, after 3 yrs.
- 1 intestinal hæmorrhage without recurrence, after 1 year.

Cases who have died of cancer—3.

- 1 extension of primary after 2 years.
- 1 extension of primary after 4 years.
- 1 pulmonary metastases after 6 years.

Of the three in whom glands developed later, the final result was as follows:

I. Case No. 28-1. Epidermoid carcinoma, right tonsil. Primary treated by radiotherapy 1928—no recurrence. Developed glands in right side of neck, 1933. Successfully treated by block dissection. No recurrence to date.

II. Case No. 30-1. Epidermoid carcinoma, left tonsil. Primary treated by radiotherapy 1930—no recurrence. Developed glands left neck five months later. These were treated by block dissection—no recurrence. Patient died of metastases in the liver 2 years later without recurrence of either the primary or the secondary.

III. Case No. 32-1. Epidermoid carcinoma, left tonsil. Referred for treatment following operative removal of primary together with dissection of neck. Four months later recurrence developed in the neck in spite of prophylactic irradiation and resisted all subsequent measures. Finally the primary also recurred and patient died within the year of extension of both.

Thus it may be said that in two of these cases surgery was the effective measure in dealing with the glandular problem, while in one case both surgery and radiotherapy failed.

2. *Cases having glandular involvement on admission: total 28.*—Class "A"—11 cases: 7 of the 11 cases in this group were treated by surgical dissection, sometimes combined with radiotherapy, either pre-operative, post-operative or interstitial. Of these, 5 remained free from recurrences in the neck and 3 are still symptom-free. Of the others, 1 case died of recurrence in the neck while the primary remained healed; 2 died of recurrences and extension of the primary only, the neck remaining healed; 1 died of recurrence of both primary and secondary. The details of the above information follow in Table III.

Class "B"—12 cases: 3 of the 12 patients were treated surgically, of whom 2 remain alive and free from recurrence, while one died of extension of the primary without recurrence in the neck. Two other patients in this group refused dissection of the glands, one at least of whom could very probably have been saved by this procedure. Nine were treated by radiological methods only. In 4 of these 9 cases the treat-

TABLE III.

CLASS "A"

1 age 87	Primary only treated. Patient did not return.	Untraced.
1 " 58	Epidermoid carcinoma. Block dissection, bilateral. No post-operative radiation. Recurrence of primary.	Died of disease 1 yr. 2 mos.
1 " 72	Epidermoid carcinoma. Block dissection right side. No post-operative radiation. Recurrence in neck. No recurrence of primary.	Died of disease 6 mos.
1 " 58	Carcinoma. Block dissection right side. Post-operative radiation ineffective. Recurrence both.	Died of disease 2 yrs.
1 " 70	Epidermoid carcinoma. Block dissection left side; interstitial radiation and post-operative radiation. No recurrence.	Alive and well 3 yrs.
1 " 54	Epidermoid carcinoma. Block dissection left side; post-operative radiation. No recurrence.	Alive and well 3 yrs.
1 " 82	Primary only treated. Patient did not return.	Died of disease 6 mos.
1 " 77	Epidermoid carcinoma. Block dissection right side. No post-operative radiation. Recurrence of primary; no recurrence in neck.	Died of disease 9 mos.
1 " 60	Negative biopsy. Primary only treated. Patient did not return. Extension of primary.	Died of disease 6 mos.
1 " 63	Transitional cell carcinoma. External radiation only to neck, ineffective. Refused dissection. Extension to neck and mediastinum.	Died of disease 1 yr.
1 " 52	Basal cell carcinoma. Telera-dium to glands ineffective. Block dissection left side. No recurrence.	Alive 1 yr.

Total, 11 cases.

ment has been successful in causing the entire disappearance of the glandular involvement and these patients remain symptom-free. One additional patient is classified as still under observation, while in one other the treatment was successful in controlling both the primary and secondary, but the patient died of mediastinal secondaries without returning for treatment of this complication. The details follow in Table IV.

Class "C"—5 cases: as will be obvious, all of the cases in this group were so advanced as to be hopeless of cure, only one patient was treated surgically, and in all cases the measure adopted was looked upon as palliative. The details follow in Table V.

Summary regarding rôle of surgery—A total of 14 cases were treated by surgical dissection, of whom 6 patients are living and 8 are dead. Ten of the number operated upon did not develop

TABLE IV.
CLASS "B"

1 age 61	No biopsy. Both primary and glands treated radiologically. Both controlled. Mediastinal involvement developed and was not treated.	Died of disease 2 yrs.
1 " 62	Epidermoid carcinoma. Radiation only. Refused dissection. Extension of both primary and secondary.	Died of disease 1 yr.
1 " 52	Transitional cell carcinoma. Block dissection left side. Interstitial radiation. No recurrence.	Alive and well 3 yrs.
1 " 73	Epidermoid carcinoma. Block dissection right side. Extension of primary.	Died of disease 9 mos.
1 " 58	Transitional cell carcinoma. Block dissection right side. No recurrence.	Alive and well 2 yrs.
1 " 51	Transitional cell carcinoma. Radiation only. Refused dissection. Extension glands.	Died of disease 1 yr.
1 " 57	Epidermoid carcinoma. Radiation only treatment. Glands controlled by teleradium.	Alive and well 2 yrs.
1 " 60	Epidermoid carcinoma. Radiation only treatment. Glands controlled by teleradium.	Alive and well 2 yrs.
1 " 67	Epidermoid carcinoma. Radiation only treatment. Ineffective. Palliation only. Extension both.	Died of disease 6 mos.
1 " 62	Epidermoid carcinoma. Radiation only treatment. Refused dissection. Under observation.	Living 18 mos.
1 " 76	Carcinoma. Radiation only treatment. Glands disappeared (teleradium).	Alive and well 18 mos.
1 " 54	Transitional cell carcinoma. Radiation only treatment (teleradium). Glands disappeared. (Also primary Ca. Breast controlled by same method.)	Alive and well 18 mos.

Total, 12 cases.

recurrences in the site of operation while in four recurrences took place. The interpretation of these facts is complicated by the added fact that 12 of the cases were also treated radiologically either before or after the operative procedure, sometimes both.

Summary regarding rôle of radiology.—

1. As a means of prophylaxis.

So many variable factors enter into the question of assessing the value of radiotherapy under these conditions as to make an accurate opinion extremely difficult to reach. In the present case one wishes to know, for example, to what extent radiation was responsible for preventing the development of glandular secondaries in those patients having no glands on admission. Eleven of the 14 received radiotherapy, 3 did not. Of

the latter one is alive and well six years later, no glands having developed. The only treatment was the radiological treatment of his primary. The second case developed glands and was successfully treated surgically. He is still symptom-free. The third died of recurrence of the primary after four years without glandular involvement at any time.

Eleven patients received radiotherapy. In 9 of these no glands developed, while glandular involvement later developed in two. In these two the radiological treatment was obviously ineffective as a prophylactic measure. How are the others to be interpreted? For the present no opinion is offered on this subject, though it is felt that 9 out of 11 is a rather high percentage to remain free from glandular complications, and suggests that there probably was some prophylactic value in this use of radiotherapy.

2. As a means of treatment of existing glands.

Twelve of the 21 patients comprising groups "A" and "B" in whom palpable glands were present were treated solely by radiotherapy. In 7 of these the glandular masses disappeared and have not recurred to date. Five of these cases were in group "B" and two in "A". In four cases in each group this method was ineffective and surgical dissection became necessary. While therefore it is evident that radiotherapy is capable of causing the disappearance of glandular masses such results are neither uniform nor certain, and there is no suggestion that the method should replace surgery, but it should be used as an alternative in some cases.

TABLE V.
CLASS "C"

1 age 88	Epidermoid carcinoma. Primary healed. Secondaries treated by radiation only. Ineffective. Extension of glands.	Died of disease 1 yr.
1 " 61	Epidermoid carcinoma. Block dissection. Resection mandible. Died of extension of primary and recurrence in neck.	Died of disease 6 mos.
1 " 59	Epidermoid carcinoma. Radiation only. Metastases in ribs and spine.	Died of disease 6 mos.
1 " 76	Epidermoid carcinoma. Radiation only. Not completed.	Died of disease 2 weeks.
1 " 70	Epidermoid carcinoma. Radiation only. Did not return (primary only treated).	Cannot trace.

Total 5 cases

The objection will of course be raised that there is no proof the glands which disappeared following radiotherapy were malignant, and since this is a controversy which cannot be settled, it is merely pointed out that in this paper when referred to as having so disappeared they have not been described as "secondaries" but merely as palpable glands. The important fact is that palpable glandular masses, in one case quite large masses were present and verified by more than one observer, and these masses have disappeared and have not recurred.

RADIOLOGICAL METHODS

In the treatment of malignant lesions of the tonsil we have been so favourably impressed by the improvement in results since full use has been made of teleradiumtherapy (*i.e.*, the 4 gramme radium bomb) that this method has now supplanted all others as the preliminary step in treatment. While making due allowance for the fact that our series of cases is small in any one year, yet it is apparent that in this disease the radium bomb finds one of its most successful fields of usefulness. During the year 1935 seven cases of carcinoma of the tonsil were treated by this means of whom 6 were entirely symptom-free at the end of the year, and the seventh became so later. No comparable results

have been obtained by us by methods previously available, and while it is not suggested that these patients are cured the record indicates a striking improvement in the therapy of this type of lesion.

As a result of this experience the method at present in use is as follows: The initial treatment consists of a carefully planned course of teleradium therapy, which includes the primary lesion and the entire area of regional lymphatics and is pushed to the point of a satisfactory tissue reaction, both in the tonsillar region and on the skin. In the majority of cases the primary lesion heals with no visible scarring. If it fails to do so, radium is applied locally by the interstitial method, using highly filtered needles.

In cases without glandular involvement, and in cases in which palpable glands are present and disappear following the treatment previously described, no surgery is undertaken. Such cases are kept under careful periodic observation and the treatment repeated as a prophylactic precaution. If, however, glands are present and fail to disappear following the first course of teleradium therapy, dissection of the neck is recommended, providing the primary lesion has been controlled or is responding favourably. The neck dissection in turn is followed by as intensive post-operative radiotherapy as the skin will tolerate without undue reaction.

BASAL ANÆSTHESIA IN CHILDREN'S SURGERY*

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BASAL anæsthesia may be considered for the purpose of this discussion as a state of unconsciousness of such degree that the patient is unaware of the events incident to his removal from his bed to the operating room and to the administration of the supplemental anæsthetic. This also implies such a degree of amnesia that there is no subsequent memory of the operation. To illustrate with a concrete instance. An interval appendectomy was performed upon a seven year old child under basal anæsthesia. When an enema was given on the fifth post-

operative day he remarked, "I know what this is. They did it to me a while ago, and I think I had an operation." The contrast between that reaction and the usual post-operative memories is striking.

Undoubtedly some of the most indelible of the unpleasant impressions of childhood are those associated with an inhalation anæsthetic, and the resultant psychic shock may well bear a causal relationship to psychological maladjustments in later life. Dogmatic statements regarding mental reactions in children, as a class, are unwise in view of the diversity of types encountered. Children may be bold or timid, trustful and confiding, or suspicious, sensitive or phlegmatic, and each type will react differently

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to environment and to stimuli. A study of such reactions does not lend itself to methods of fixed physical measurements or accurately controlled factors, but certain observations are sufficiently common to be of significance.

A study of post-operative conditions at the Children's Orthopædic Hospital revealed a definite correlation between post-operative acidosis and pre-operative emotional disturbance, the index of acidosis being the degree of acetoneuria. Those children who approached operation in a calm, unfrightened state usually had minimum post-operative morbidity and little if any acetoneuria, whereas those who were markedly disturbed pre-operatively usually had a stormy recovery with a high degree of acetoneuria of two or more days' duration. In observations of this nature it is important to differentiate between the child who is actually unafraid and the one who is outwardly calm but inwardly terror-stricken. While the character of the operative procedure was no doubt a factor the intensity of emotional upset was found to have a much more direct influence. Acetoneuria may be interpreted as evidence of increased metabolic activity with protein destruction and depletion of reserve, and is associated with increased activity of the autonomic nervous system and the endocrine glands. These physical reactions are manifest by physical signs.

What may be said of the psychic reactions? Gwathmey¹ has observed the development of stuttering in one child and the necessity of prolonged psychiatric care in another as a consequence of pre-operative fear and lack of sedation. Beverly,² in an excellent recent article, draws a striking picture of the all too prevalent lack of attention to the pre-operative environment of a child. In substance he says that the child is brought to the hospital with false assurances and persistent prevarication; his eyes, ears and nose are assailed by strange and usually disagreeable stimuli; impersonal and uninterested attendants separate him from the parents upon whom he has always relied for protection and security; he sees instruments which his little playmates may have fiendishly described as being used to cut off arms, legs and even heads; and, finally, he is held down on a table by the superior brute force of two or three adults while he passes screaming and struggling into suffocating unconsciousness. No child ever undergoes such an experience without being thoroughly frightened, and it is impossible to estimate the psychic damage and

sequelæ. One of the characteristics of human memory is that it is mercifully short for unpleasant experiences, but such an ordeal may well be a factor in a subconscious distrust of parents, favouring domestic maladjustments, or a fear of doctors and hospitals which may later delay medical consultation at a critical time, or influence a decision to turn to cultists.

The general surgeon, 80 to 95 per cent of whose patients are adults, is necessarily concerned with the problems of adult surgery. His initiative, ingenuity and time are quite properly directed primarily toward solving these problems rather than those of children's anæsthesia, which he usually considers of minor importance, the anæsthetic merely representing a more or less irritating delay to the primary incision. Anæsthetists, pædiatric nurses, and those of us who are constantly confronted with the problems of infancy and childhood, however, have long been keenly aware of the inadequacy and defects of anæsthesia as usually employed in children's surgery, of the undesirable aspects of post-operative recovery, and of the unwholesome mental distortions and deviations which often result. Given a skilful, tactful anæsthetist, a child who has not been ruined by a previous badly administered anæsthetic and a surgeon who is not over-anxious to conserve a few minutes of his time, it is possible in practically all instances to induce satisfactory anæsthesia with any suitable inhalation anæsthetic agent. How rarely, however, do we meet such a happy combination! And how often is one of the major results of an operation the development of another anæsthephobe!

Pre-anæsthetic medication was developed to combat pre-operative difficulties, and it has been carried to a high degree of perfection, particularly for those adults whose nerves are irritated by toxins, or whose mental reactions are so disturbed as to render appeal to reason difficult. Strangely enough, in childhood when the nervous mechanism is being constantly bombarded by showers of strange impulses, and mental reactions are so undeveloped as to render appeal to reason impossible, pre-anæsthetic sedation was at first little used and even considered contraindicated.

With the development of the intravenous administration of barbiturates the long-awaited ideal anæsthetic for children seemed to have arrived, but again there was delay because the manufacturers could supply no information as to the dosage for children, and the earlier clinical

reports warned against its employment in the two extremes of life. The reason for such a warning was evidently fear of possible unfavourable reactions or unfamiliarity with children rather than actual observation of untoward results, as more extensive use has since proven. Now the child may remain quietly in bed talking normally with his parents and experience only the slight inconvenience of a needle puncture or an enema, with either of which procedures he is probably already familiar. Not until he has passed easily and quickly into a deep, quiet slumber is he moved to the operating room. The mental shock of parental separation and the physical shock of restraint and semi-asphyxia are entirely eliminated. Let me call it to your attention also that the psychological effect upon the parent is a most happy concomitant of this method of anaesthesia, as any one of us can well attest who has stood by while his own child has taken even the most skilfully administered inhalation anaesthetic.

Basal anaesthesia or narcosis may be induced by the various barbiturates administered by mouth, by vein, or by rectum; or by tribromethanol (avertin) or paraldehyde administered rectally. They have been termed irreversible anaesthetics, and have been considered uncontrollable because absorption can not be halted at any desired point as with the inhalation anaesthetics. This undesirable feature has been obviated to a great extent in the more recently developed forms which after absorption are rapidly broken down and excreted as non-toxic substances. An overdosage sufficient to cause depression and inhibition of respiration does not affect the heart, and thus it is possible to use respiratory stimulation or artificial respiration effectively during the comparatively short period required for excretion of the excess anaesthetic. Coramine intravenously is a most effective antidote. If an idiosyncrasy to barbiturates is suspected a small test dose may be given by mouth a day or two previous to the operation.

The rectal anaesthetics possess the advantage of employing a familiar procedure and not requiring a needle puncture with the occasional difficulty of entering a small or obscure vein. They are time-consuming, however, as they must be given slowly and should be started 20 to 30 minutes before the child is to go to the operating room. Where time of induction is a factor the quickly acting intravenous anaesthetics are to be preferred. Post-anaesthetic excitement

occurs more frequently after the barbiturates than after avertin or paraldehyde, but it is of short duration and easily controlled by morphine.

It has been stated that basal anaesthesia is contraindicated in operations on the upper respiratory tract, but Gwathmey reports that in tonsillectomies the safety factor is increased by adequate pre-anaesthetic medication, followed by a proper anaesthetic sequence.

Deaths have been reported following the use of avertin (Brown, Maddox), but under careful analysis they are found either to have occurred early in the development of these agents, or to have been due to faulty technique. They have generally followed the attempt to produce total instead of basal anaesthesia. Maddox³ estimated that avertin had been used 1½ million times up to the date of his survey over two years ago, and the reported fatalities have been very few.

Medical literature of the past few years has contained a considerable number of references to intravenous and rectal anaesthesia, both basal and total, and many of these mention briefly that they are also of value in children. Recently, however, reports have begun to appear dealing entirely with the use of these agents in children, and the early vague fears and theoretical objections are disappearing. The profession in the United States seems to be slow to give up pre-medication by morphine, which does not eliminate psychic disturbance, and also rather tardy in following the lead of the British as regards basal anaesthesia in children. The demand for its use will no doubt come from the paediatricians and paediatric nurses rather than from the surgeons.

The intravenous barbiturates most frequently used at present are sodium amytal, pentothal, and evipal. They are quickly-acting, and the latter two are especially rapidly excreted. They occasionally cause post-operative restlessness and excitement, but nausea and vomiting are markedly reduced. Paraldehyde has been used rather extensively in Great Britain, but avertin is generally preferred for rectal administration. The barbiturates are also well tolerated and absorbed by the rectal mucosa, and may be used in this manner with excellent results.

Basal anaesthesia is contraindicated in toxic and cachectic children, and rectal administration should not be used in the presence of rectal or colonic inflammation. Healthy infants and young children tolerate full doses for their weight as well as older children and adults, the reason being, no doubt, that the younger the child, the

more active are the physiological processes, and hence the more rapid the elimination of the anæsthetic.

Personal experience with basal anæsthesia in infants and children, extending over more than four years, has been highly satisfactory, the only adverse observations being those already mentioned. The mental reaction of children who have been subjected to multiple operations and who have had the opportunity to make comparisons has been uniformly and enthusiastically favourable. They make little or no complaint of the discomforts or restraint incident to the operation, but are most vigorous in their protests against inhalation anæsthesia. The following remarks are typical: "I don't mind an operation, but I hate that ether"; "Please let me have that needle anæsthetic"; "If I have to come back may I have my anæsthetic by an enema again?" "I don't care how many operations I have if I may have that kind of an anæsthetic"; and so on.

The use of the barbiturates has been followed by post-anæsthetic excitement in about 10 per cent of our cases but this has always been easily controlled. There has been respiratory depression of varying degrees associated with the use of avertin, but only once to an extent requiring stimulation, the cause in that instance bring too rapid administration. There have been no deaths and no occasions for anxiety other than the very temporary one just mentioned.

Details of physiological action and of administration are important but have been purposely omitted as coming more properly within the scope of a technical paper.

LIPOIDOSIS CUTIS ET MUCOSÆ.—According to R. N. Tripp this disease was discovered independently by Wiethe in 1924 and Urbach in 1929, and its study was placed on a firm base by their joint investigation of nine cases in four families. In these cases, as well as a tenth described by Tripp, there were scattered deposits in the skin and mucous membranes of a lipoid, soluble in hot alcohol or acetone, and apparently a phosphatic lipoid closely related to, if not identical with, lecithin. Clinically the most prominent feature was hoarseness, due to laryngeal lipoidosis, appearing in the second year of life

Basal anæsthesia should not supplant all other forms of pre-anæsthetic medication, nor is it suitable for all cases, for anæsthesia to be best must be individualized. It is, however, ideal for the great majority of cases in the field of surgical pædiatrics. Children have for many years not only survived the usual types of anæsthetics but have grown to be healthy adults, and, no doubt, will continue to do so, due to their wonderful ability to adjust themselves to adverse conditions, but should we make this characteristic an excuse for giving them anything less than the best?

Let me urge upon you in behalf of all children who may in the future come to the operating table that you do your part in developing the popularity of this humane procedure by requesting basal anæsthesia whenever it is not definitely contraindicated. The pædiatrician must lead the way. Both his clientèle and the profession at large will appreciate his tactful insistence upon thoughtful consideration of his little patients in a matter which so definitely affects not only their present physical comfort but also their future psychic development. Someone has well said "Anæsthesia is not a courtesy, it is a right". Permit me in closing to adapt that quotation to the present subject by saying that basal anæsthesia for children is not a courtesy; it is their right.

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at the latest; a familial incidence was well established. On the skin white nodular masses and hyperkeratotic lesions were present, on the face and proximal interphalangeal finger-joints in all cases. Infiltrations were common on and in the tongue and epiglottis. The condition, which is allied to xanthoma and necrobiosis lipoidica diabetorum, improves if treated with restricted carbohydrate intake and small doses of insulin. In several patients biochemical tests have shown a latent diabetic tendency.—*New York State J. of Med.*, April 15, 1936, p. 619. Abs. in *Brit. M. J.*

PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE*

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PREGNANCY complicated by heart disease is a grave condition for both mother and child. The maternal mortality is high and premature birth is frequent. In our experience at the Toronto General Hospital the maternal mortality has varied, in previously reported cases, from 8.4 to 2.3 per cent. Eastman¹ estimates the maternal mortality at 8 to 5 per cent, and states that on that basis 1,000 women die annually in the United States from heart disease complicating pregnancy. An even more dramatic emphasis of the seriousness of this complication of pregnancy is made by Hamilton and Kellogg,² who state that 20 per cent of the maternal deaths at the Boston Lying-In Hospital over a period of four years were due to heart disease. W. Schuman³ states that the second highest cause of maternal mortality at the Sinai Hospital, Baltimore is cardiac disease.

In 1933 the writer in conjunction with Prof. W. A. Scott⁴ reported on a series of patients suffering from rheumatic heart disease and pregnancy delivered at the Toronto General Hospital. The problem of myocardial disease and pregnancy was considered in various aspects and certain general conclusions were drawn. Two of the conclusions resulted in broad changes of policy at our clinic in regard to the observation and management of the pregnant patient with heart disease. The first led to the establishment of a combined prenatal and cardiac clinic which has permitted personal consultations between cardiologist and obstetrician and a continuity of observation of all heart cases by one obstetrician and cardiologist. As far as practicable all labours are conducted by the same obstetrician. The second conclusion led to a radical change in the methods of delivery. In the series reported in 1933 Cæsarean section was the method of delivery in 46.3 per cent of the cases. We concluded that this high incidence of Cæsarean section was unwarranted and should be reduced.

The purpose of this paper is to give our present opinions in regard to heart disease and pregnancy,

and to report a new series of 35 deliveries. Included also, is a report of 11 pregnancies terminated because of rheumatic heart disease.

During the past three years 35 patients suffering from rheumatic heart disease and pregnancy have attended the combined prenatal cardiac clinic at the Toronto General Hospital. These patients have been divided into three groups according to the severity of their heart disease and are very similar in comparison to the cases previously reported in 1933. Table I presents

TABLE I.
SEVERITY OF THE HEART DISEASE

	<i>Previous Series</i> 41 Cases <i>Primiparae 15</i> <i>Multiparae 26</i>	<i>Present Series</i> 35 Cases <i>Primiparae 15</i> <i>Multiparae 20</i>
Slight or no impairment of exercise tolerance...	16 cases	15 cases
Moderate to severe impairment of exercise tolerance.....	16 cases	14 cases
Failure.....	9 cases	6 cases
Total.....	41 cases	35 cases

such a grouping and comparison of the two series. Group 1 includes those patients with no or only slight impairment of exercise tolerance. Group 2 includes those with moderate to severe impairment of exercise tolerance, and Group 3 includes those who had cardiac failure. The patients were classified after delivery and many who would have been in Group 1 early in pregnancy were finally classified in Group 2. All patients who developed failure did so after the fourth month.

The methods of delivery for the two series of cases are shown in Table II. The incidence of spontaneous births is practically the same for

TABLE II.
METHOD OF DELIVERY

<i>Type of Delivery</i>	<i>Previous Series</i> 41 Cases	<i>Present Series</i> 35 Cases
Spontaneous.....	39.0% (16 cases)	45.7% (16 cases)
Forceps.....	14.6% (6 cases)	51.5% (18 cases)
Cæsarean section and sterilization..	46.3% (19 cases)	2.8% (1 case)

*From the Department of Obstetrics and Gynaecology, University of Toronto.

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both series. The great difference occurs in the incidence of forceps deliveries and Cæsarean section. Forceps were employed nearly four and a half times as frequently in the second group as in the first, while the incidence of Cæsarean section was reduced from 46 to 2.8 per cent. Both series of cases are small, nevertheless they show that practically identical results were obtained in similar cases by conservative as compared with radical methods of delivery. It seems reasonable to suppose that the constant employment of a serious abdominal operation in a larger number of cases would lead to a higher mortality than would simple forceps delivery.

There was one death from heart failure in both series. In the first series the death occurred twenty-four hours after a forceps delivery, while in the second series the death occurred twenty-seven days after induced labour and spontaneous delivery.

The complications of labour are shown in Table III. Premature birth occurred 7 times,

TABLE III.
COMPLICATIONS OF LABOUR

Complication	No. of Cases	Primiparæ	Multiparæ
Premature births.....	7	3	4
Post-partum hæmorrhage	1	0	1
Excessive post-partum bleeding.....	4	2	2

Average duration of labour in primiparæ, 18 hours.

or in 20 per cent of the cases, which is characteristic of pregnancy complicated by heart disease. The constant danger of post-partum hæmorrhage in the cardiac patient is emphasized by one case of severe post-partum hæmorrhage and 4 cases of excessive post-partum bleeding. The average duration of the first stage of labour in primiparæ, 18 hours, is mentioned as it is usually stated that labour is rapid in the patient suffering from heart disease.

In our experience over 90 per cent of heart disease complicating pregnancy is rheumatic in origin. The most common valvular lesions are mitral stenosis and insufficiency, although aortic insufficiency is not unusual. The diagnosis of heart disease and the estimation of the ability of the heart to stand the added strain of pregnancy are both frequently difficult. The large hypertrophied breasts of pregnancy interfere with the percussion of the heart borders, and the raised diaphragm, which occurs fairly early in

pregnancy, results in the rotation of the apex of the heart outwards, further adding to the difficulty of estimating the degree of cardiac hypertrophy. The murmurs also frequently change as the pregnancy progresses. It is not unusual to find at one examination a definite mitral diastolic murmur, only to discover that it has disappeared when the patient is next examined. Shortness of breath and dependent œdema, common symptoms of heart disease, are frequent accompaniments of normal pregnancy, particularly during the later months. These difficulties of diagnosis are all minimized in the early months of pregnancy, and are further evidence of the value of early prenatal examination and observation.

More than usual care should be taken in the routine heart examination of the pregnant patient or many cases of heart disease will be missed. A large percentage of patients suffering from this complication of pregnancy have no symptoms of heart disease (15 out of 35 in the present series), and hence nothing to direct attention to careful examination of the heart. An enquiry in regard to past attacks of rheumatic fever or chorea should be a routine question, and when such a history is elicited particular care should be exercised in the examination of the heart.

The progressive nature of rheumatic heart disease warrants particular emphasis when considered in relationship to pregnancy. A patient, 20 years of age, suffering from rheumatic heart disease may withstand the strain of pregnancy and labour without cardiac embarrassment, yet a few years later pregnancy may result in failure and death. In other words, the history of uneventful past pregnancies is no indication that a subsequent pregnancy will not cause a cardiac breakdown. In a previously reported series of 10 patients⁴ who developed failure during pregnancy, 7 were multiparæ who had experienced relatively normal pregnancies up to the one causing the cardiac breakdown.

MANAGEMENT OF THE PREGNANT PATIENT
WITH HEART DISEASE

The management of the pregnant patient suffering from heart disease can be conveniently discussed under three headings:—The management during the prenatal period, during labour, and during the puerperium.

Management during the prenatal period.—The first requisite here is frequent observation. The value of such prenatal examination is particu-

larly well emphasized by Lamb⁵, who reports a 2.2 per cent mortality where adequate prenatal care was carried out, compared with a 20 per cent mortality in patients who did not receive prenatal observation. The observation must be frequent. Our procedure is to have the patient visit the clinic twice a month until the eighth month, and each week from then on. We advise admission to hospital seven to ten days before the expected date of confinement for rest and observation. The reason for such frequent observation is to discover early cases that are developing progressive impairment of exercise tolerance or impending failure. Once cardiac insufficiency has occurred, the maternal mortality is more than doubled, and if labour occurs during failure the mortality is about 50 per cent.

Special advice should be given in regard to hours of rest. The physiological strain of pregnancy on the heart can best be compensated for by increased rest and limitation of exercise. Fourteen hours a day in bed are necessary for all cases, and this should be increased as the pregnancy progresses or if the patient is unusually dyspnoic. At the earliest sign of cardiac failure absolute rest in bed is necessary.

The physiological gain in weight during pregnancy is an added burden to the heart and should be controlled by suitable restrictions in diet. If the patient is obese efforts should be made to prevent any gain in weight, and in the co-operative patient an actual reduction in weight may be obtained.

The importance of avoiding intercurrent respiratory infection should be stressed, and when slight colds occur the patient should remain in bed.

The occurrence of signs or symptoms of the late toxæmias of pregnancy warrant hospital treatment. J. Corwin *et al.*⁶ have reported an increased incidence of toxæmia in the pregnant patient suffering from heart disease, but this has not been our experience. However, the occurrence of even mild degrees of hypertension and albuminuria should be viewed with alarm.

Management during Labour.—The occurrence of labour in the patient suffering from heart disease may be looked upon as a final test of the diseased myocardium, yet it need not be unduly feared. If a patient goes through pregnancy without developing cardiac insufficiency then she is very unlikely to develop it as result of normal labour. It is often amazing how well a patient stands a prolonged first stage of labour

without cardiac embarrassment. Cæsarean section has been advocated for a number of years as a method of delivery to relieve the heart from the strain of labour. While the incidence of Cæsarean section has been markedly reduced in our clinic we do feel that it has definite, if restricted, indications, in cases of heart disease. It is justified in patients who have serious myocardial damage and where long or difficult labour is anticipated with increased risk to the baby. The type of Cæsarean section performed depends to a great extent on the degree of circulatory embarrassment that is present. Classical Cæsarean section can be performed with the patient flat on the table or with the shoulders raised. This position is preferable to the Trendelenburg position required for the low Cæsarean. If, however, there is little circulatory embarrassment and the patient is not dyspnoic, the low section, because of greater safety and less post-operative distension, should be employed. Sterilization should be done at the time of operation.

During the first stage of labour the chief attention should be directed to the relief of pain and anxiety and the promotion of relaxation and rest. Heroin in twelfth of a grain doses, in our experience, has proved the most satisfactory sedative. Morphine and hyoscine are not used because of their occasional exciting effect. In the more prolonged labour adequate intake of fluids and carbohydrates is important to prevent acidosis.

The exhausting expulsive efforts of the second stage of labour should be eliminated by the use of forceps in the full-term deliveries, and episiotomy alone when the child is premature. The anæsthetic of choice is ether combined with oxygen to prevent cyanosis.

Premature labour is a common occurrence and the incidence of excessive post-partum bleeding and hæmorrhage is definitely increased. Sudden collapse after delivery may occur. This should be anticipated by the application of a tight abdominal binder with pad after delivery and the early return of the patient to bed in the Fowler position.

Management during the Puerperium.—The cardiac patient requires close observation during the puerperium, as frequently two to three days after delivery a period of exhaustion occurs and the patient appears more ill than at any time during the pregnancy. The average patient requires three weeks in bed and the more severe cases, a correspondingly longer time. There is no

reason, if the patient is not too exhausted, why she should not nurse her baby.

THE TERMINATION OF PREGNANCY

A discussion of pregnancy complicated by heart disease would be incomplete without considering the indications for the termination of pregnancy. During the past five years, at the Toronto General Hospital, 11 patients have had their pregnancies terminated because of rheumatic heart disease. The indications for termination are shown in Table IV and require little

TABLE IV.

INDICATIONS FOR TERMINATION OF PREGNANCY
11 CASES

<i>Indication</i>	<i>No. of Cases</i>	<i>Primiparae</i>	<i>Multiparae</i>
Impending failure.....	4	0	4
Failure before or during pregnancy.....	6	1	5
Toxic vomiting plus heart disease.....	1	0	1
Total.....	11	1	10

comment. The four patients who had their pregnancies terminated for impending failure were all multiparae who, despite hospital treatment, failed to improve sufficiently to warrant the risk of carrying the pregnancy to the period of viability. The history of previous myocardial failure or the occurrence of failure during pregnancy were the indications for termination in six cases. One patient had her pregnancy terminated because of the added complication of pernicious vomiting.

Just as it is impossible to lay down positive dogmatic rules for the management of the pregnant patient suffering from heart disease so it is impossible to be positive as to all indications for the termination of pregnancy. Termination of pregnancy is indicated in any patient who has had myocardial failure before becoming pregnant. There is no reason to believe that a heart which has already failed will stand the added strain of pregnancy. The occurrence of myocardial failure during pregnancy is also an indication for termination, but only after recovery from the failure has occurred. Operative interference with pregnancy during failure is almost uniformly fatal. However, once recovery from failure has occurred the pregnancy should be terminated, as the progressive embarrassment of the heart caused by the growing pregnancy may cause another

and fatal attack of cardiac insufficiency. A slight delay in termination, however, is indicated if the pregnancy is close to the period of viability.

A number of patients will, early in pregnancy, develop increasing impairment of their exercise tolerance, often to a marked degree. A certain number of these require termination, and it is in this type of case that the judgment of both cardiologist and obstetrician experienced in the problem of heart disease and pregnancy is of particular value. The parity of the patient presenting such a picture is an influencing factor in arriving at a decision for termination. With the primiparous patient anxious to have a baby an effort should be made to carry the pregnancy to the period of viability. The multipara, the mother of young children, is a very important member of the home and community, and more radical recommendations are justified. Similarly, the amount of rest a patient can obtain during pregnancy is an important factor. This depends on the size of her family, household duties, responsibilities and her ability to cooperate.

The method of termination of the pregnancy depends largely on two factors, first, the severity of the heart disease, and, second, the duration of the pregnancy at the time of operation. Table V shows the methods used in the present

TABLE V.
METHODS OF TERMINATION OF PREGNANCY
11 CASES

<i>Method</i>	<i>No. of Cases</i>	<i>Duration of Pregnancy</i>	<i>Results</i>
Dilatation and curettage.....	2	under 3 months	satisfactory
Supravaginal hysterectomy.....	7	4 to 6 months	"
Abdominal hysterectomy and sterilization.....	1	3 months	"
Bag induction.....	1	4 months	"
Total.....	11		

series of 11 cases. The operation of choice is one that combines termination and sterilization with the minimum of shock and disturbance to the patient. In our experience supravaginal hysterectomy has met these requirements with considerable success when the pregnancy is between four and six months. As many patients with heart disease eventually develop menorrhagia removal of the uterus is of prophylactic value. Early in pregnancy dilatation and curettage is a relatively easy and non-shocking oper-

ation, and while sterilization is not accomplished, it is nevertheless, the operation of choice. Abdominal hysterotomy and sterilization conserves the uterus, which is of doubtful value in these cases, but, according to M. Stutz,⁷ of the Zurich Women's Clinic, is followed by an incidence of fatal pulmonary embolism thirty times as great as that after full-term delivery. In severe cases of heart disease on the verge of failure, where any operative procedure is hazardous, the introduction of a hydrostatic bag to induce labour is a conservative procedure.

The question of future pregnancy for the patient with rheumatic heart disease must be carefully considered. The intelligence and the ability of the patient to cooperate will determine whether sterilization or only contraceptive advice is necessary. Patients who have had failure or who have moderate impairment of exercise tolerance should be advised against further pregnancies. For the group of patients who have no symptoms or only slight impairment of exercise tolerance, the deciding factor is frequently the economic status of the patient. The higher incidence of myocardial failure developing during pregnancy in a group of public-ward patients compared with a private group has already been mentioned. This difference can be partly explained by the increased rest, greater comfort of home life, and freedom from worry that the private patient as a rule enjoys. Many factors have to be considered, not the least of which is the parents' own view on the matter. It is only fair to the patient to point out the added risk she faces in a contemplated pregnancy, which can be conservatively stated at five times the normal.² We do not believe that sterilization is an indication for Cæsarean section. It can be performed with less risk to the patient when she is not pregnant. Vaginal sterilization is preferable in most cases.

It has not yet been definitely shown that

pregnancy *per se* shortens the life of a group of patients suffering from heart disease. The added responsibilities and increased work associated with the care of young children in the home may be of equal importance. Our impression however is in agreement with the conclusion of Gilchrist and Murray-Lyon⁸ that repeated pregnancies tend to shorten life and increase the risk of death from cardiac failure.

CONCLUSIONS

1. Rheumatic heart disease is a serious complication of pregnancy.
2. Prenatal observation by cardiologist and obstetrician is necessary for the proper management of these cases. The aim of prenatal management is to anticipate and prevent cardiac failure.
3. If cardiac failure does not occur during pregnancy it is very unlikely to develop as a result of normal labour.
4. The employment of conservative methods of delivery in rheumatic heart cases is recommended, while the indications for Cæsarean section are limited.
5. For the majority of patients further pregnancies are inadvisable and termination of pregnancy is frequently justified because of rheumatic heart disease.

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GNORRHOEAL VAGINITIS: RESULTS OF TREATMENT WITH DIFFERENT PREPARATIONS AND AMOUNTS OF OESTROGENIC SUBSTANCE.—In treating gonorrhoeal vaginitis, R. M. Lewis and Eleanor L. Adler found that oestrogenic substance in ethylene glycol given hypodermically was relatively effective when used in large doses: 2,400 international units daily. Eight hundred international units daily proved disappointing. The use of vaginal oestrogenic suppositories (originally 600 international units and later 1,000) proved very effective. Clinical improvement, cessation or great diminution of discharge is nearly always noted after from fourteen to eighteen days of treatment. The administration of oestrogenic substance changes the reaction of the vaginal

secretions from neutral or alkaline to acid. This, the authors believe, is the major factor in eliminating the gonococcal infection. The acidity of the vaginal secretions is easily measured and provides a sure guide by which one can determine whether or not dosage is adequate. Of thirty-three consecutive cases of gonorrhoeal vaginitis in children treated with oestrogenic suppositories, thirty yielded negative smears in an average of 20.7 days. Two required twelve weeks of treatment. Five cases are listed as recurrences. No ill effects were encountered. The method is safe and harmless, and the most effective method known for the treatment of gonorrhoeal vaginitis in children.—*J. Am. M. Ass.*, 1936, 106.

COMPLICATIONS OF ARTIFICIAL PNEUMOTHORAX

(A REVIEW)

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THIS review is an attempt to reach an opinion as to the frequency and severity of the complications of artificial pneumothorax. It is important that one should have an opinion on this point because of the gradually growing tendency to induce pneumothorax in cases of minimal disease and without a preliminary period of a few months' observation.

Pleural Adhesions.—Table I shows how frequently various operators have failed to induce pneumothorax because of adhesions.

TABLE I.

Author	Number of cases	Number in which pneumothorax was impossible
1	200	90
2	79	25
3	275	85
4	105	24
5	600	120
6	71	21
7	443	112
8	150	37
9	207	53
10	462	185
11	51	12
12	149	47
13	200	34
14	139	54
15	250	29
Totals	3,381	928

Case selection rather than the technique of induction is responsible for the considerable variation in experience shown by the above Table.^{16,17,18} It has been frequently observed, and may be accepted as fact, that the greater the duration of disease, the more likely are adhesions to be present. A most striking demonstration of this is afforded by Turner and Collins' series of 40 early and minimal cases with 100 per cent effective collapse.¹⁸

When pneumothorax has been successfully induced there is, as Table II shows, a large percentage of cases in which complete pneumothorax is prevented by adhesions.

TABLE II.

Author	Number attempted	Number with only partial collapse
7	443	232
19	492	183
9	207	75
11	51	37
20	275	125
Totals	1,468	652

Percentage
with only
partial collapse
= 44

This is a high figure and an important one to remember, because the results of treatment are considerably less worth while when only a partial pneumothorax is possible. Again contrast this with Turner and Collins' series.

When thoracoscopic severance of adhesions is contemplated, the surgeon's chief fear is the presence of lung parenchyma in these adhesions; this has been found in two-thirds of one series.²¹

It is quite impossible to tell in advance by x-ray or by any other means whether adhesions will prevent effective collapse or not. Pneumothorax may be successful even when the x-ray reveals a visible thickening of the pleura, and may be impossible when no warning of the presence of adhesions can be detected prior to operation. Once a lung has been collapsed and allowed to expand, re-induction is frequently impossible, but not invariably so.

Pleural Effusion.—The frequency of this complication in the experience of several operators is shown in the following Table:—

TABLE III.

Author	Percentage frequency of pleural effusion	Total number of pneumothorax cases
22	25%	63
23	16%	50
24	"over 50%"	101
2	25%	1,400
5	"nearly all cases at some time"	480
17	42%	?
7	28.8%	143

At least half of these effusions are very small in amount and transient, so that part of the variation in experience shown by Table III may be due to variation in the frequency with which these cases are observed fluoroscopically.

In spite of the large number of theories which have been suggested to explain these effusions, there is sufficient evidence to show that they are tuberculous exudates in all or almost all cases.^{24,25} Their incidence is greatly reduced in minimal disease, in chronic disease, in low pressure pneumothorax, and by taking every precaution not to damage the underlying lung with the needle point. Conversely, they become much more common and more severe in extensive disease, acute disease, high pressure pneumothorax, and are almost invariable following the accidental production of a pleuro-pulmonary fistula. It is probable that their usual causes are trauma to the lung by the needle point, tearing or separation of an adhesion, or the natural evolution of tuberculosis upon the surface of the lung or pleura. Bard's demonstration of pleuro-pulmonary fistulæ in almost all cases with exudate is especially convincing.²⁶

Effusions most frequently appear without causing symptoms, but any of the symptoms of an ordinary pleurisy may be present. They have no important effect upon the prognosis provided they remain clear.²⁷

Purulent Effusions.—In general, the greater the volume of the effusion, the more acute its onset, and the longer it persists, the more likely it is to become purulent. This transformation of clear fluid to pus has been observed in 12 per cent of 75 effusions²⁴, and in 23 per cent of 186 effusions.²⁸

Some cases of tuberculous empyema, however, originate as such. The total incidence of

TABLE IV.

Author	Number of pneumothoraces	Number of empyemas
23	50	1
29	30	1
30	62	3
31	250	26
5	480	58
27	344	6
9	154	7
32	151	32
33	142	9
34	226	12
28	265	42
7	331	6
Totals....	2,485	203

empyema in pneumothorax cases has been reported by various authors as in Table IV.

Empyema is always a worrying complication, but many of these cases are so benign that the clinical course of the disease is not disturbed, and with proper treatment many patients recover without much difficulty, or carry pus in the chest for many years without apparent harm. This, however, is never true of the cases with mixed infection. Of Hayes' 32 cases, 18 had died at the time of his report, and only 1 was accounted well. Of Swezy and Schonbar's 7 cases 4 had died and only 1 was well. Of Peters' and Woolley's 9 cases, 3 were in good condition at the time of the report and 4 had died. Some authors have had better success, however. In Matson, Matson and Bisailon's 58 cases the complication was found to have no serious consequences unless open drainage was established. McKinney³⁵ had only 1 death in 8 cases, the remaining 7 being restored to full working capacity. One must make some estimate, and it appears likely that less than half the empyema cases when properly treated by aspiration and irrigation have serious consequences. Since the incidence of empyema is 8 per cent, empyema leading to death or serious and prolonged additional disability will probably occur in less than 4 per cent of all pneumothorax cases. Most of the serious cases are secondarily infected.

Empyemas nearly always occur in cases with far advanced tuberculosis and a high degree of collapse.

The frequency of secondary infection empyema in pneumothorax therapy is variously reported as in Table V.

TABLE V.

Author	Number of pneumothoraces	Number of mixed infection empyemas	Died
36	331	4	3
31	250	8	7
37	254	7	?
34	226	2	?
Totals.....	1,061	21	

The percentage incidence of mixed infection empyema is therefore about 2. This is included in the 8 per cent total incidence of empyema, and accounts for most of the 4 per cent of serious empyemas.

Most of these mixed infections are thought to be autogenous in origin and to result from lung rupture. They are frequently associated with bronchopleural fistula.

Hæmothorax and Hæmorrhage from the Chest Wall.^{22, 38, 39, 11} These are rare complications. The reviewer found only 8 reported cases. One, associated with spontaneous pneumothorax, resulted in death. No doubt minor degrees of hæmorrhage into the pleural cavity are not uncommon but produce no consequences of clinical importance.

Contralateral Effusion.—A review of the literature to 1929 resulted in the finding of 32 reported cases.⁴⁰ The complication is really to be considered as a coincident happening probably unrelated to pneumothorax therapy, and has usually been of little importance unless associated with the extension of contralateral disease.

Spontaneous Pneumothorax.—The incidence of this complication has been reported very variably, depending on the observer.

TABLE VI.

Author	Number of pneumothorax cases	Number of "spontaneous" pneumothoraces
41	1,145	10
42	196	4
43	120	7
11	38	3
31	150	4
9	207	8
5	480	16
23	50	1
44	150	4
17	143	10
22	63	4
Totals.....	2,742	71

The percentage incidence from Table VI is 2.6. There is little doubt that "spontaneous" pneumothorax is much more frequent than this, but, resulting in no serious consequence, is overlooked.

Most of these cases are not really "spontaneous". A better word is "accidental". They may be due to a needle injury, in which case symptoms may be absent or trivial and usually delayed a few hours or minutes. Such injuries will be more frequent at initial insufflations. Or an adhesion may be torn from the lung, when symptoms may be more severe, perhaps resulting in a secondary infection empyema or in valvular pneumothorax.

Mortality from accidental or spontaneous pneumothorax results from empyema or from valvular pneumothorax whose constantly increasing pressures produce circulatory embarrassment and surgical emphysema. Valvular pneumothorax, however, may be classed as a very rare

complication—probably rarer than fatal gas embolism—and the majority of spontaneous or accidental pneumothoraces are harmless.

Contralateral and Transmediastinal Pneumothorax.—With an artificial pneumothorax on one side a spontaneous pneumothorax on the other has serious possibilities. Fortunately it is very rare. In 1919 Duboff could find no case in the literature. Since then Burrell⁴⁵ has reported 2 cases, both fatal. Walsh's case was also fatal.⁴⁶ The reviewer found 5 cases reported in which air escaped from the pneumothorax side into the contralateral pleural cavity. Four of the 5 recovered.^{47, 48, 9, 50, 51}

Similar in nature and consequences are those cases of bilateral artificial pneumothorax in which spontaneous or accidental pneumothorax occurs. Since we believe these accidents are fairly common in unilateral pneumothorax they may be expected to be twice as common in bilateral pneumothorax, and no doubt will more readily produce symptoms. The majority of the reported cases have recovered.^{52, 53, 54, 55}

Mediastinal Hernia.^{28, 56, 57, 58, 59, 60, 61}—This term was introduced by Dumarest and Brette. It means a bulging of the mediastinal parietal pleura across the midline through the anterior weak spot of Nitsch, as a rule, thus enlarging the pneumothorax cavity at the expense of the opposite lung. The condition is usually detected by x-ray examination, especially by fluoroscopy, when the herniated portion is seen to be larger with expiration and smaller with inspiration. These hernias occur in young people with healthy, unfibrosed, mediastinal septa. If the pneumothorax pressures are kept low they become smaller, disappear, and do not recur. They are generally harmless. One case is reported, however, of death due to pressure upon the heart and cardiac failure.⁶⁰ This complication is unusual, but not really rare, and almost never gives serious trouble. The hernia has however been known to rupture into the opposite pleural cavity, producing a transmediastinal pneumothorax.

Pollock and Marvin have recently reported some cases which they believed to show a collection of air in the mediastinum with bulging of each mediastinal pleural septum to its respective side, and without subcutaneous emphysema in the neck. They believe that cases previously called mediastinal hernia were really mediastinal emphysema or pneumatocoele. They may be right. Their paper is quite convincing and should be read by those interested.

Subcutaneous Emphysema.^{22, 62, 63, 64, 65}—This is a very frequent accompaniment of the initial insufflation, and is almost always no more than a minor annoyance. It is quite unusual after an ordinary refill. It probably results as a rule from tearing the parietal pleura when a blunt trocar is pushed through it. Air may reach the mediastinum by way of the sub-pleural tissues and cause severe dysphagia or crepitations felt beneath the skin of the base of the neck in front. Subcutaneous emphysema may follow a spontaneous pneumothorax of the valvular type, when it becomes extreme, the whole body being swollen with subcutaneous air. Such cases are usually fatal, but are very rare.

Fibrin bodies in the Pneumothorax Cavity.^{66, 67, 68, 69, 70, 71}—Single or multiple balls of fibrin, usually about 4 cm. in diameter, are occasionally discovered by x-ray loose in the pleural cavity or attached in that part of the pleural cavity most dependent in the usual position of the patient. The patient may be conscious of the internal knocking about of these balls, but usually they are unnoticed and of no clinical importance. A history of effusion is almost always present, and it is thought that the balls consist of fibrin, left unabsorbed when a serofibrinous effusion disappears. Some have been thought to be fibrin from an incompletely absorbed hæmothorax. Some appear to persist indefinitely. Some at least are absorbed completely.

Intercostal Pleural Hernia.—A unique case is reported by Matson, Matson and Bisailon.⁵

Pneumoperitoneum.^{72, 73, 74, 75, 76}—This is a rather rare complication. It may be produced by the operator who pushes his needle through an unusually high diaphragm; or air may leak from the pleural cavity through an opening in the diaphragm—probably as a result of congenital defect. Only about 12 cases have been reported to date, and none have produced more than a transitory discomfort, though occasionally pneumoperitoneum has frightened the operator into discontinuance of pneumothorax therapy. Theoretically and usually paradoxical manometer readings will be obtained with the needle point in the abdominal cavity, but this has not been an invariable experience. Neither Zink nor Gerber found paradoxical readings. It is worth remembering too that paradoxical readings may rarely be obtained from the pleural cavity. It is possible that some of the cases reported as pneumoperitoneum may have been subdiaphragmatic rather than intraperitoneal collections of air.

Pleural Reflex or Gas Embolus or Both.—Alarming symptoms at the time of operation may be classed as syncopal, convulsive or paralytic. The possible causes for alarming symptoms at this time are:—a simple faint; extreme nervousness; reaction to local anæsthetic; pure coincidence, e.g., insulin reaction, cerebral thrombosis; pleural reflex; gas embolus to the brain or coronary arteries of heart. Convulsive or paralytic symptoms are usually blamed on either gas embolus or pleural reflex, depending on the faith of the operator. Syncopal reactions and very sudden deaths have often been ascribed to pleural reflex. But some believe that all severe reactions not due to coincidence are due to gas embolism, and that pleural reflex either does not exist or is of no real importance. This school of thought is the one most acceptable to the writer.

The evidence for and against the various theories is too extensive to produce here at length. Certain facts however should be known. (1) In nearly all cases, possibly in all, there are adhesions which keep the lung close to the chest wall. (2) In many cases symptoms will be accompanied by bloody sputum as evidence of lung injury. (3) These accidents are more common at initial insufflations than at refills. It seems probable that these accidents are associated always with injury to the lung itself or to adhesions crossing the pleural cavity. No precaution therefore, is too great to adopt in order to avoid lung injury so far as is possible. When recovery occurs from these accidents it is always complete; no residual paralysis persists. Death may be delayed for as long as 7 days, but once consciousness is fully regained recovery is certain.

The frequency with which these accidents have occurred is shown by the following Tables.

TABLE VII.

Author	Number of pneumothoraces	Number with alarming symptoms	Deaths
77	1,400	1	0
78	300	2	1
79	202	1	0
45	344	2	1
5	480	19	2
9	207	3	1
20	275	0	0
80	100	1	0
81	418	10	3
Totals	3,726	39, or 1.1%	8, or 0.2%

TABLE VIII.

Author	Number of punctures	Number with alarming symptoms	Deaths
78	8,258	2	1
30	900	0	0
82	7,000	0	0
45	2,332	2	1
83	1,986	9	1
84	12,700	16	7
5	12,000	19	2
85	2,000	11	1
86	10,000	0	0
81	12,000	10	3
Totals . . .	69,446	69, or 0.1 %	16, or 0.02 %

Puncture of the Heart.^{42, 80, 83}—This is a very rare event, from which the patients have all rapidly and completely recovered.

Neuralgia and Neuritis.^{87, 88}—Patients not uncommonly have complained of pain in the neck, in the face or shoulder, down the arm, or in the side of the chest following refills. Some authors have reported such cases as "neuralgia" or "neuritis". These cases are at least generally explicable as due to referred pleural pain, possibly resulting from stretching of an adhesion. It is an unimportant though occasionally an annoying complication.

Hæmoptysis.^{89, 90}—Spitting of a little blood may follow within a few minutes or hours of insufflations in which it is possible that the needle has entered the lung. Apart from this accident however there are rare cases in which pneumothorax appears to precipitate or aggravate true hæmoptysis. Matson, Matson and Bisailon⁸⁹ have noted that such hæmorrhage may come from the contralateral lung, and urge less compression if this be so, and more compression if the hæmorrhage comes from the collapsed lung.

"Refil Reactions".^{42, 91, 92, 93, 89}—These are unusual, but are characterized by the occurrence a few hours (4 to 24) after each of several successive refills of fever and possibly of chills, sweats and chest pain. The symptoms persist for 24 to 48 hours. They appear to occur usually in persons who have a pleural effusion, or who have suffered an acute pleurisy at some time. As a rule, but not invariably, they occur rather late in the course of treatment. No satisfactory explanation of their occurrence has been provided, but reactions can often be prevented in cases in which they occur by insisting that the patient stay in bed for 24 hours after each refill, which should be administered to the patient in his bed. They are not of much importance, and should

not often lead to discontinuance of pneumothorax treatment.

Displacement of the Diaphragm.—Ayeock⁸⁴ suggests this as the cause of digestive disturbances following pneumothorax therapy. The reviewer adds the suggestion that this may bear some causal relationship to the rare cases of acute dilatation of the stomach occurring in pneumothorax cases.

Atelectasis.—By atelectasis one means absorption of air from the lung or a part of it following obstruction by exudate, by kinking, or by pressure, of the bronchi supplying the area of lung affected. Atelectasis is easily produced in a lung by anything which interferes with respiratory movement, from myasthenia gravis to chest injury. It must and does occur in artificial pneumothorax, and will occur in some degree in all cases if adhesions be not present to help keep the lung expanded and moving. It is the end-result of all cases of complete pneumothorax and many cases of partial pneumothorax. Atelectasis is what produces fibrosis in the collapsed lung. It does so because the bronchus to the atelectatic lung, being obstructed, does not rid itself of secretions, and so non-tuberculous infection becomes active, producing fibrosis and even bronchiectasis in the collapsed part of the lung. Atelectasis therefore is the chief factor responsible for failure of the lung to re-expand, or for its smaller volume when expanded. Adhesions which prevent atelectasis are therefore not absolutely without their redeeming feature. Partial pneumothorax, in which considerable lung movement is permitted to continue, is often found not to result in atelectasis, and this is a good argument in favour of this form of collapse therapy. It is not possible to say how frequently atelectasis leads to serious troubles. If there be a price to pay for atelectasis it is nearly always worth paying.

Metastatic Tuberculosis.—Pneumothorax therapy does not completely prevent the spread of tuberculosis to other organs of the body—a spread which must as a rule be hæmatogenous. Peters²⁹ reports that extrapulmonary foci developed or became manifest during the course of pneumothorax treatment in 6.4 per cent of 275 cases. Neuer⁸⁵ has claimed that pneumothorax therapy actually favours the spread of tuberculosis to other organs. An apparently hæmatogenous spread of tuberculosis to the opposite lung has been observed by several. A predisposition to hæmatogenous spread due to pneumothorax

treatment seems distinctly contrary to one's experience, but a doubt has been raised here which, so far as the reviewer can discover, has not been satisfactorily resolved. Here is a study which someone should undertake.

The Contralateral Spread of Pulmonary Tuberculosis.—Cooper and Stallings⁸¹ have a report which is particularly valuable because they distinguish between disease originally unilateral and disease originally bilateral. Their Table follows.

TABLE IX.

	No. of cases on pneumothorax	Unilateral Tuberculosis				Bilateral Tuberculosis					
		No. of cases	Improved	Un-improved	Spread to other lung	No. of cases	Improved	Un-improved	Other Lung		
									Worse	Better	Unchanged
Satisfactory Collapse	205 49%	104 57%	54 52%	50 48%	15 14%	101 43%	56 55%	45 45%	21 21%	28 28%	52 51%
Unsatisfactory Collapse	213 51%	78 43%	22 28%	56 72%	7 9%	135 57%	38 28%	97 72%	41 30%	19 14%	75 56%
Total . . .	418	182 43%	76 42%	106 58%	22 12%	236 56%	94 40%	142 60%	62 26%	47 20%	127 54%

Thus they find a spread to a previously normal lung in 12 per cent of 182 pneumothorax cases and extension of disease in the better lung in 26 per cent of 236 cases. Rist⁹⁷ finds that contralateral extension accounts for 75 per cent of the deaths that occur under pneumothorax treatment.

We know that pulmonary tuberculosis tends rapidly to become bilateral if pneumothorax is not induced, so rapidly that the majority of cases are bilateral and far advanced when first they present themselves to the physician. It seems unfair therefore to blame pneumothorax for causing contralateral extension of disease. Unfortunately, however, the reviewer has been unable to find a study of the bilateralization of disease in which pneumothorax cases are compared with control cases. Another doubt has been raised here which needs to be resolved, and here is another chance for someone to make a valuable study. But one must feel that since it can be thoroughly proven that pneumothorax has a favourable influence on the whole, it cannot on the whole favour the spread of tuberculosis.

*Tuberculosis of the Larynx*⁹⁶.—Pneumothorax almost invariably has a favourable effect on this complication when present, and the abolition of bacilliferous sputum by pneumothorax will tend to prevent its development.

Acute Dilatation of the Stomach.—This is to be classed as one of the rarest complications of artificial pneumothorax. Shore's⁹⁸ case in 1926 is the only one in the literature that one could discover, but the reviewer had one in his practice. Both were fatal and undiagnosed in life. The chief symptom in both was extreme dyspnoea. There was no vomiting or abdominal pain in my case, though both were present in Shore's. This complication should be suspected in any case of

severe dyspnoea. Once suspected, it is probable that abdominal enlargement will be observed.

Diabetes Mellitus.—This offers no obstacle to pneumothorax treatment, but on the contrary is an indication for the early induction of pneumothorax, in order to shorten the period of toxæmia which will aggravate the diabetes.

Pneumonia and Influenza.—Burnand⁹⁹ had 20 pneumothorax patients with influenza during the epidemic of 1918-19. Six of these died of "flu"; the remainder recovered, and their tuberculosis was none the worse for their experience. Rickman¹⁰⁰ had 2 pneumothorax patients with pneumonia, and in both the tuberculosis was adversely affected.

Pneumonia of the contralateral lung is a serious situation, and, since pneumonia is a fairly common disease, its possible occurrence is a valid argument against carrying on pneumothorax an unnecessarily long time.⁴²

Pregnancy and Delivery.^{101,102}—The patient with pneumothorax suffers no added risk according to the fairly large series of cases so far reported.

*Digestive Disturbances and Loss of Weight.*⁹
^{103,94}—These occasionally occur following pneumothorax therapy but are rarely of much clinical importance. Three theories as to their cause have been suggested, namely, displacement

of the mediastinum, or of the diaphragm, or a metabolic disturbance due to deficient oxygenation of the blood. The mechanical causes appear to be the most important.

SUMMARY

Complications of pneumothorax which lead to serious consequences do so as a rule by causing empyema.

The incidence of empyema having serious consequences is about 4 per cent of all pneumothoraces. The incidence of other serious complications is probably less than one half of 1 per cent, if all are added together, so that serious and probably fatal complications of artificial pneumothorax may be expected in not over 5 per cent of all pneumothorax cases. This is not a minimal figure and may be considerably too high, for Matson, Matson and Bisailon¹⁹ say of their large group, "of this series less than 2 per cent died of complications related to the pneumothorax treatment".

Since the great majority of empyema cases occur in persons with far-advanced tuberculosis, the risk to an early case is probably less than 2 per cent from all complications of pneumothorax treatment.

In deciding whether or not to induce pneumothorax to such cases this risk is to be balanced against what the individual patient stands to gain by this treatment. The above figures disregard the faint possibility that pneumothorax may actually favour the spread of contralateral or metastatic tuberculosis.

It is to be noted that in 27 per cent of cases pneumothorax treatment has been found impossible because of adhesions, and in another 44 per cent the pneumothorax produced was made only partially effective because of adhesions. Adhesions are very much less frequent, less numerous, and less troublesome in disease of short duration and little extent.

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NOTE: The complete bibliography may be obtained on application to the Academy of Medicine, Toronto.

M. Loretì records four cases of typhoid fever which occurred during the Abyssinian campaign in Italian soldiers who had been inoculated against the disease. The attack in each case was so modified by inoculation as to be mistaken in two cases for influenza and in one for rheumatic fever. Three developed intestinal perforation, of whom two died, and the fourth patient died

from intestinal hæmorrhage. Loretì points out that every physician and surgeon, especially in war time, should consider the possibility of a typhoid perforation in the presence of an acute abdominal emergency, although the patient has been only slightly feverish and the symptoms are indefinite.—*Rif. Med.*, June 20, 1936, p. 558. Abs. in *Brit. M. J.*

EMBOLISM AND SUDDEN THROMBOSIS OF THE ARTERIES OF THE EXTREMITIES

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SUDDEN occlusion of one of the large arteries of an extremity does not occur often, but when it does it is serious and often results in some permanent disability to the patient, and even may cause loss of the limb. The seriousness of the results is not attributable to the occlusion of the artery *per se*, but rather to the resultant ischæmia of the peripheral tissues which is consequent on the cutting-off of the blood supply. Thus, the results vary with the site of occlusion, the available collateral circulation, the duration of ischæmia and, to some extent, with the rapidity of occlusion.

As ischæmic tissues die within a few hours after the blood supply has been shut off completely, an early diagnosis of arterial occlusion in a limb must be made if one is to attempt to reestablish adequate blood flow to the part and prevent necrosis. In order to make this diagnosis a correct knowledge of the signs and symptoms of sudden arterial occlusion is necessary.

ETIOLOGY

The specific etiological factor in the sudden occlusion of an artery of an extremity is not always self-evident, and a careful study of the available facts must be made in attempting to arrive at a correct diagnosis. In the presence of the factors to be described subsequently, the diagnosis is often fairly simple. Unfortunately, however, one is not always able to determine any obvious cause, and the conclusion arrived at is a result of logical deduction based on all available information. Fortunately, the treatment of sudden arterial occlusion does not demand an accurate knowledge of the cause.

Emboli which involve the acral arteries originate somewhere in the proximal portion of the arterial tree, in the left side of the heart, or in the pulmonary veins, except the occasional paradoxical embolus, which occurs when a patent foramen ovale is present. The pulmonary veins

are rarely the source of emboli.¹ Mural thrombi in the heart, which are the result of endocardial lesions, are acknowledged generally to be the most frequent source of arterial emboli. Bull, of Riks Hospital, Oslo,¹ in 6,140 necropsies found that 243 (about 4 per cent) of the patients had mural thrombi, and in 9 of these thrombi likewise were found in the aorta. Willius² said that about 25 per cent of the patients who die of heart disease have had emboli at one time or another. Willius recognized that factors other than endocarditis played important rôles in the formation of cardiac thrombi (potential emboli); he mentioned such factors as enlargement of the cavities of the heart and disturbances of rhythm. A feeling is developing among some cardiologists that sudden restoration of a normal cardiac cycle in an arrhythmic heart does not predispose towards embolism. Bull found, at necropsy, that the majority of patients who had cardiac thrombi also had pathological changes in the cardiac valves or in the myocardium, and that in all cases in which there were cardiac thrombi there was a greater or lesser dilatation of the various cavities of the heart. The proximal arteries are less commonly the source of emboli. The aorta is the chief source in the proximal arteries, particularly in cases in which emboli are associated with, or are the result of, some specific cause, such as damage to the intima, which may be caused by an aneurysm, arteriosclerosis, or trauma.

Thrombosis of an acral artery actually occurs secondarily to some primary process in the vessel or blood, such as embolism, degenerative processes in the wall of the vessel, inflammation, trauma, or increased coagulability of the blood.

In thrombo-angiitis obliterans sudden occlusion of the peripheral arteries occurs in about 11 per cent of the cases; the percentage is about the same in thrombo-arteriosclerosis obliterans. Why the thrombosis occurs suddenly in this small percentage of cases is not known. In periarteritis nodosa the thrombosis occurs over a period of

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days, but, generally speaking, the condition is more or less acute, and for this reason it has been included in this group. In severe infections, such as peritonitis, pneumonia, septicæmia, and so forth, a bacterial arteritis may play a major rôle in causing thrombosis, but another factor that must be considered seriously is increased coagulability of the blood, which is the result of the infective process. Blood dyscrasias such as thrombophilia, as described by Nygaard and Brown,³ which tend toward the formation of thrombi, also must be thought of in the differential diagnosis.

Thrombosis may occur in an extremity following operation, and in trying to discover the specific cause there are many factors that have to be considered. Extension of thrombosis from small arteries close to the field of operation to the larger arteries may be the explanation in some cases. However, this does not explain the sudden thrombosis of a vessel distant from the site of operation. In these cases it is possible that increased coagulability of the blood plasma, particularly if the patient is debilitated, may be one of the factors, and stagnation of the blood, which is attributable to inactivity of a limb subsequent to an operation, is probably one of the accessory causal factors when associated with unusual conditions present at the time of operation, such as severe infection, arteriosclerosis, and so forth.

In the presence of gunshot wounds, stab wounds, cervical ribs, or other similar conditions which may injure an artery the thrombosis of that vessel may be attributed to the factors mentioned. Greenspan has described carcinomatous involvement of pulmonary arteries, and it seems logical that carcinoma could invade the wall of an artery elsewhere in the body and cause sudden thrombosis of that vessel.

PATHOLOGY

The pathological changes which occur in a limb that is the site of a sudden arterial occlusion may be divided into two groups: (1) those which occur in the limb, and (2) those which occur in the vessel at the site of obstruction. The changes which occur in the limb are the result of the ischæmia rather than the result of the thrombus or embolus. They will, in consequence, vary from simple trophic changes in the skin, nails, and hair, in cases of mild thrombosis, to massive dry or moist gangrene in cases of more severe thrombosis. The changes in the vessel in the region of

the occlusion vary according to the nature of the occluding factor. Thus, in the presence of inflammation, such as thrombo-angiitis obliterans, periarteritis nodosa, and bacterial arteritis, signs of inflammation are present microscopically and even macroscopically. In cases in which arterial occlusion is not associated with inflammation, as in the presence of an aseptic embolus or thrombosis of hæmic origin, the reaction is mild.

Consequent to the formation of a thrombus, and providing the wall of the vessel has not undergone excessive degeneration, according to Muir, fibroblasts and small blood vessels which invade the clot from the intima and vasa vasorum cause organization of the clot, and often recanalization of the lumen to a greater or lesser degree.

In experimental work on embolism, Gosset, Bertrand and Patel⁴ demonstrated that septic emboli caused a marked inflammatory reaction around the clot and in the wall of the vessel at the end of twenty-four hours. Aseptic emboli, in a series of studies made up to eight days after the onset, showed what the authors believed to be aseptic necrosis of the wall of the vessel. This was caused partially by interference with the blood supply of the vascular wall as a result of pressure by the embolus itself. Organization and fibrosis of the clot were well developed at the end of eight days.

SYMPTOMS

In 1911, Buerger described sudden arterial occlusion, and described the typical embolic phenomena as being associated with sudden pain, blanching and coldness of the limb. Since then, few other descriptions have been given that have not described the symptoms of sudden arterial occlusion, with particular reference to embolism, as being similar to those described by Buerger. However, a broader view must be taken when entering into a discussion of the symptoms of acute arterial obstruction, as the symptoms frequently are not acute and the condition is not always accompanied by pain.

When an acral artery for any reason becomes completely occluded in an acute manner there is a diminution in blood supply to the distal part of the limb, which is the result of the blockage of the main vessel and the associated arteriospasm in the collateral vessels. Consequent on this sudden anæmia there are phenomena which are attributable to the diminished blood flow to the peripheral bones, muscles, nerves, and other

structures of the limb. These phenomena are readily recognized as associated with ischæmia, even though their specific etiological factor is not always apparent. Similarly, it is impossible to explain the reason why some manifestations are apparent in one case and not in another, or why there is a total absence of signs and symptoms, as in an unusual case of acute occlusion described by Buerger.

In a previous study by the author and E. V. Allen⁵ it was shown that the onset of symptoms occurred suddenly in 48 per cent of cases. The remaining 52 per cent had an onset lasting from one to several hours before the maximal severity of the symptoms was present. In 54 per cent of cases, pain, which rarely was of great severity, was the initial complaint, and in 44 per cent of cases the pain came on suddenly. Other symptoms of less frequent occurrence were tingling, tenderness, cramps, itching, pallor, and burning, in the order of their frequency.

There was no definite order of onset or apparent causal relationship in the presence of these individual symptoms, and they occurred singly or in varying combinations with each other, one or the other predominating in different cases. Thus, an attempt to describe the clinical symptoms would be difficult, other than to say that the presence of any of these symptoms should necessitate a further study of the case, particularly in relation to the objective findings of the cardiovascular system.

The examination of the patient usually shows that there are few if any signs of shock unless the unusual severe type of pain is present. The facial colour is fairly good, the pulse is a little faster than it normally is, but, unless cardiac decompensation is present, the rate is not alarming. The oral temperature is within normal limits, and the patient is usually wide awake, alert, and somewhat apprehensive. The appearance of the limb readily demonstrates that some pathological change has taken place. The normal colour is absent and the limb is blanched, blotched, or sometimes slightly cyanotic below the region supplied by the available collateral circulation around the obstruction. The veins are collapsed, the limb is frequently immobile, and its general appearance is very aptly described as lifeless.

Palpation reveals the skin to be cool and moist, and no pulsations are felt in the arteries peripheral to the site of obstruction. Tests for sensation, muscular power, and neurogenic reflexes ordi-

narily show diminished or absent responses. It is a definite clinical impression that the degree of anæsthesia, paresis and diminution of reflexes depends on the degree of ischæmia, and that the amount of response in an affected limb is in proportion to the blood supply, providing the response is not produced by structures situated in a region which has a good blood supply and which is proximal to the anæmic portion. Assuming this impression to be true, then the amount of voluntary muscular movement might be used as a rough index of the amount of collateral circulation functioning. That this is logical is borne out by an observation made by Allen¹⁰ that the complete absence of digital movement in the involved extremity probably means that little or no collateral circulation is present, and that the chances for recovery of the limb are slight if paresis persists a few hours.

If the blockage of the artery is complete, and if there is insufficient collateral circulation to maintain life in the tissues, then within the first few hours the sensations of pain, numbness, and tingling usually diminish or disappear altogether, and the patient complains only that the limb is "dead" and that he is unable to move it. If pain, tingling, and movement are present after the first few hours, they are either in the proximal portion of the limb, where some circulation is present, or there is sufficient collateral circulation to the more distal parts to allow for the continued viability of some nerve fibres at least. After a lapse of several hours a retrograde flow of blood occurs through the venous channels, which progresses slowly peripherally, and which frequently changes the colour from pale whitish to a blotchy bluish purple. This retrograde seepage is of no significance and does not indicate the restoration of circulation.

Death of the tissues is the ultimate outcome if the cutting-off of the circulation is not compensated for quickly. This necrosis manifests itself as gangrene. If, however, sufficient circulation is reestablished the limb may recover to the extent where it is a functioning member once more, although it seldom recovers sufficiently so that there are no residual symptoms, such as varying degrees of claudication.

DIAGNOSIS

As the deleterious effects of arterial occlusion are the result of ischæmia of the tissues, the final results of obstructing the blood supply to the

limit will vary in accordance with the degree and the length of time the blood supply is diminished. Thus the diagnosis obviously must be made early if benefit is to be derived from treatment. In order to make the diagnosis early it is not necessary for the physician to have an accurate and widespread knowledge of the symptoms and pathology of sudden arterial occlusion. Rather, all that is necessary is the knowledge that the symptoms are sufficiently varied, so that if some unusual occurrence directs his attention to the limb he will carry out a thorough examination, particularly of the acral arteries, and will rely on the examination rather than on the history for the diagnosis of occlusion.

An embolus most frequently is arrested at the bifurcation of an artery where there is a sudden diminution in the size of the vessel. The bifurcation of the femoral and popliteal arteries is the most common situation in the legs, and the bifurcation of the brachial artery is the most common situation in the arm. Absence of pulsation below a given point in an artery is indicative of arterial occlusion, if a normal arterial tree always is assumed to begin with. If this absence of pulsation is associated with abnormal pallor and decreased surface temperature, then the diagnosis of recent arterial occlusion is justified. Other findings are confirmatory but not individually diagnostic.

The differential diagnosis lies chiefly with anomalies of the vascular tree, in which the arteries of the extremities do not follow their normal course, and with arteriospasm. In the former condition there are no other significant findings which indicate an associated pathological closure. In the latter condition, however, the differentiation is not so simple. Küttner and Baruch⁶ described a case in which the ankle was injured by a bullet and the posterior tibial artery was thought to be thrombosed, as signs of obstruction were present. While the wound was being repaired, the vein was found to be injured; the artery was uninjured but in a state of spasm which completely occluded its lumen. Montgomery and Ireland reported two cases of traumatic arteriospasm of the brachial artery, and gave an excellent review of the reported cases of this condition. Ordinarily, a careful study of the possible etiological factors and the subjective and objective findings will lead to the correct diagnosis.

PROGNOSIS

The prognosis in sudden peripheral arterial occlusion is not always good, as I have found that gangrene developed in about half of the cases studied in which there was sudden occlusion. Of those patients who did recover there were very few who did not have at least some residual symptoms, such as claudication, trophic changes, and so forth.

TREATMENT

The treatment of an extremity subsequent to the sudden occlusion of an acral artery has changed considerably in recent years as a result of a more thorough knowledge of the course of events. This knowledge, which has been gained by careful clinical and experimental investigations, is the basis of present-day treatment.

Gosset, Bertrand and Patel⁴ observed arteriospasm in the region of an artificially produced embolus. They also noted that the surface temperature (as indicative of circulation of blood) was restored to normal after several hours in many cases. Mulvihill and Harvey,⁷ in experimental ligations of the femoral arteries of dogs, found that the usual decrease in the surface temperature of the limb could be prevented or promptly compensated for by paralysis or section of the sympathetic nerves to the part. Herrmann and Reid⁸ have shown that alternating suction and compression on an affected limb has a beneficial effect, and they claim that when there is more or less sudden occlusion of one of the major arteries of an extremity the early use of this form of treatment practically eliminates the possibility of gangrene. Denk⁹ reported excellent results in cases of sudden peripheral arterial occlusion in which the patients were treated with papaverine hydrochloride.

One can realize that the measures instituted should all tend to increase the inadequate collateral bed, which is thought to be inadequate as a result of arteriospasm in addition to occlusion. As spasm of the arteries or inadequate dilation seems to be the result of activity of the sympathetic nerves, then procedures that will paralyze these nerves are indicated; these procedures comprise spinal anæsthesia, brachial block, or deep general anæsthesia. Vasodilators, such as papaverine hydrochloride, in doses of $\frac{1}{2}$ grain (0.032 gm.) administered intravenously, may be tried. Alcohol, 0.5 c.c. per kilogram of body weight, is also beneficial, as shown by Brown and Cook. Other vasodilators, such as mecholin and theobromine have been shown to have definite clinical value. Great care must be taken of the limb itself, and it should be wrapped in cotton and placed under a cradle with the temperature not more than 105° F. It should be remembered that devitalized tissues burn more readily than do normal tissues.

If a prompt response to these attempts at vasodilatation does not occur, then surgical intervention may be considered if the obstruction is the result of an embolus. Mosny, Dumont, and Labey performed the first successful embolectomy in 1911; the next year, Key performed a similar operation. Since then, there have been many arteriotomies performed. In 1929, A. W. Allen¹⁰ reviewed the literature and found that only 25 to 30 per cent of the embolectomies were successful. In 1933, Danzis¹¹ collected 119 reports of embolectomies from the literature, of which 41 per cent were immediately successful. In these cases, 25.5 per cent of the patients died from embolism which occurred two to eight months after operation. Inasmuch as the surgical technique of embolectomy has been described in an admirable manner by Pemberton,¹² A. W. Allen,¹⁰ Labey, and others, it seems unnecessary to discuss it further in this paper.

The reason for the failure of embolectomy is most frequently the development of a secondary thrombosis. This may occur almost immediately, or not for some time. Ipsen found no evidence of thrombosis two days after the obstruction occurred, whereas Lindberg found a secondary thrombus, 86 cm. long, as early as twelve hours after the onset of the embolism.

Key said that no benefit ordinarily was obtained with operation after forty-eight hours, and that in cases in which operation is performed within forty-eight hours of the onset of the embolism good results may be expected in 45 per cent where the operation is performed one to ten hours after the onset; in 21 per cent in which

it is performed ten to fifteen hours after the onset; and in only 10 per cent in which it is performed fifteen to forty-eight hours after the onset.

CONCLUSIONS

1. The symptoms of sudden arterial occlusion are extremely variable. The common conception that severe pain, which ensues suddenly, is the chief manifestation is misleading.
2. Sudden occlusion of an acral artery demands early institution of adequate treatment.
3. Treatment should consist of attempts to overcome arterial spasm and to enlarge the collateral arterial bed. Embolectomy may be tried early in selected cases.

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KLEIN'S CANCER REACTION.—H. Horster reports from the University Hospital of Würzburg investigations he has conducted into the reliability of the reaction described by G. Klein of Oppau in September, 1934. After studying Klein's technique Horster arranged to send him samples of blood from Würzburg, and within a year the blood of 215 patients had been examined in Klein's laboratory. There were 75 cases of malignant disease, 125 cases in which tumours could be excluded, and 15 cases in which the clinical diagnosis was doubtful. It was found necessary to exclude from the final analysis several of the cases because they were complicated by adventitious circumstances such as fever, hæmorrhage, constipation, cachexia, anacidity, or retention of food. Other circumstances confusing the issue were the ex-

hibition of certain drugs and x-ray examination. After all the cases thus complicated had been eliminated there remained 45 patients suffering from some tumour; among them were 39 positive Klein reactors and 6 which were negative. Among the 91 patients not suffering from tumour were 83 giving a negative Klein reaction and eight a positive reaction. Horster concludes that Klein's tumour reaction does not at present represent a valuable contribution to the diagnosis of malignant disease, largely because of the facility with which extraneous circumstances obscure the issue. To this negative verdict he adds the rider that Klein's reaction promises so much of theoretical and scientific interest that he intends to continue his investigation of it.—*Deut. med. Woch.*, March 10, 1936, p. 460. Abs. in *Brit. M. J.*

THE PSYCHOLOGICAL DISTINCTION BETWEEN THE VARIOUS TYPES OF SCHIZOPHRENIA

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INTRODUCTION

THERE is a tendency in studying psychotic cases to restrict attention to the enumeration of symptoms for the purpose of categorical classification and the estimation of prognosis. Even granting that we acknowledge the existence of mental conflicts, complexes, symbolic manifestations, etc., we do not utilize these conditions systematically to explain the type of reaction which the patient is showing. Even granting also that we distinguish certain personality types, we still do not utilize these, except in a very general way, to explain the nature of the disorder. That is to say, our study is largely symptomatic, rather than etiological or interpretive. It is not the purpose of this paper to go into the details of the symptoms in the various groups, but rather to offer some generalizations regarding the psychological processes involved in the development of the various types of schizophrenia. Since we admit that there are different types of this disorder it is surely not too much to suppose that there must be some distinguishing factors in the etiology which lead to the various manifestations.

The study of psychology teaches us that the activity of the normal mind may be analyzed into various factors. In the following pages the growth in the mind of four different processes is discussed, and an effort is made to show that the four types of schizophrenia represent disorders of these four processes.

PART I.

THE SIMPLE TYPE OF SCHIZOPHRENIA INTERPRETED AS A DIMINUTION OF INSTINCTIVE FORCES

(a) *Normal growth of instinctive forces.*—One of the most universal attributes of the animal mind is a tendency to display interest and

energy. According to the view of most psychologists these are expressions of instinctive forces. In the human infant the development of these forces is gradual. At first he responds mechanically to certain stimuli, such as the opportunity to suckle. Some such experiences bring pleasure and he becomes interested in them and eager to play his part; others he dislikes, and his energy is directed towards avoiding them. The various instincts gradually become more manifest, curiosity, anger, fear, constructiveness, play, etc., etc., and they form the basis of most of the child's activity. As time goes on his innate tendencies become elaborated and directed into more useful lines. He becomes interested in work, he assumes duties and responsibilities, he becomes ambitious for the future and directs his life accordingly.

The course of these developments is naturally dependent on the experiences to which the individual is exposed. His interest is aroused in some lines and thwarted in others. His ambition should develop in keeping with his opportunities; otherwise it is unlikely to be fulfilled. One should note that there is considerable variation in the amount of energy displayed. Individuals differ considerably, some being naturally active while others are more listless. Also, the same person will display much more interest and energy along some lines than others, and even from time to time the amount of energy he displays towards the same subject will vary. Within certain limits, however, such variations are normal.

(b) *Diminution of instinctive forces.*—In the simple type of schizophrenia there appears to be an abnormal diminution of interest and energy. This, after all, is one of the most natural reactions to any unsatisfying existence. If a person is dissatisfied with his circumstances in

life, if he is discouraged by his failure to attain his desires, is not the simplest reaction that of giving up the struggle? The forces which should drive him on diminish or atrophy; he begins to disregard his duties, responsibilities and ambitions, and follows the line of least resistance. One might cite examples of diminution of instinctive forces occurring in so-called normal people as a result of adverse circumstances. Take, for instance, the disappointed lover who loses interest in life for a long time, and possibly never regains the zest which he formerly experienced; or take the wife who, when married to a brutal husband, gradually loses her energy, pugnacity, determination, ambition, even her self-respect, and subsides into a humdrum life of listless submission; or take the ambitious young man who fails repeatedly to obtain the promotion he deserves, and who finally feels discouraged, stops struggling, and accepts a routine occupation which offers a bare livelihood.

In the case of the simple schizophrenic the changes are more severe. He so disregards his responsibilities to himself and others that he is no longer able to maintain any normal position in the community. His earning power decreases, and, with it, his standard of living. His dependents suffer, he loses his friends, and he drifts along. To many people such consequences would be intolerable and would increase the mental conflict. But to this type of individual the consequences mean nothing; his sense of values has changed to such an extent that he has no ambition for higher achievements, and he does not regret his condition nor blame either himself or others for it. His emotions, which should be aroused by his plight, become flattened and his interest and energy diminish. When he reaches the haven of a mental hospital he accepts a placid uneventful existence, and may adopt a simple routine occupation with neither ambition nor resentment. It is to be noted that in this type of case associations are coherent as far as they go, but thinking is reduced to a minimum. The patient's imagination is not active consciously or subconsciously, and there is little tendency to develop delusions or hallucinations. Failure of interest and energy, such as occur in this type, may be regarded as deteriorating factors. The progress of the disorder may become arrested at any point, but recovery of interest and return to normal is uncommon.

(c) *Example of simple type.*

(Case No. 5506 P.M.H.).—This patient is a woman who was admitted on January 5, 1932, at the age of 42. There was no history of nervous or mental disease in her family. She was born in Ontario, and her infancy and childhood were said to have been normal. She attended school until 17, when she failed in one subject in third year high school. She tried nursing, but was discharged over some affair with a disreputable man. Later she worked in a sanatorium. At 22 she married a man who was unattractive and unequal to her in refinement. Her married life was probably not happy. She spent much time reading and day-dreaming about the stories she read, and she neglected her housework. She is said to have been sensitive, stubborn and lazy, but not shy. She had very restricted interests. Some sexual irregularities occurred while she was single.

Her present illness probably started before 1926. In that year she spent six weeks in a mental hospital and is said to have been very erotic. Following this she returned home but never adjusted well. She separated from her husband and she and her three children lived on the allowance she received from him. She made no attempt to improve her circumstances. There was a gradual loss of interest. She became more and more negligent in her housework. She shirked her responsibilities and did not appear to realize that she had any. Even when one of her children was in diabetic coma she neglected his treatment and appeared quite unconcerned.

When admitted to hospital she was in good health. She has been quiet and placid, and has worked steadily in the nurses' home. She is satisfied and entirely lacking in ambition, and shows no initiative to depart from the simple routine of her monotonous life. She shows a shallow mechanical smile when spoken to, and answers questions rationally but without emotion. When not occupied she sits by herself. There is evidence that her thought processes are of a very simple type. She has no delusions or hallucinations.

PART II.

HEBEPHRENIC TYPE OF SCHIZOPHRENIA INTERPRETED AS A DISORGANIZATION OF THE MIND

(a) *Normal organization of the mind.*—As an individual's mind develops from infancy to maturity it becomes more and more completely organized. Association is an important factor in this development. Things which occur together or in sequence, or which have similarities, become associated in the mind so that the thought of the one tends to recall the thought of the other. As a result of these associations things take on meanings. The individual learns to appreciate the relationship of various things, their significance, their relative values. It is important to recognize that feelings and emotions determine to a considerable extent the significance which things have for an individual—hence love is blind. Some things become associated with pleasure, some with pain, some with love, some with hate, some with fear, and so on. As various emotions all become associated successively with the same object, such as one's mother, the object develops a complex emotional

significance which is termed a "sentiment". One experience will emphasize one relationship, while another experience may emphasize another relationship. For instance, when the mother feeds her child he associates a certain form of pleasure with his mother; at another time, when she punishes him, he associates fear and pain with her. Now these two associations might conflict were it not that the child should also associate with each case the circumstances in which it occurs. Thus he finds that his mother is good to him when he is good, and strict with him when he is bad. In other words, when adequate and accurate associations are developed, the relationships which result in the mind are consistent; and while opposite emotions may be associated with the same object they do not conflict, because they are reasonable and appropriate to the circumstances. This is to be expected in ordinary life, because one's environment is more or less consistent, being dependent on the laws of nature and the laws of man, and therefore one's experiences are consistent.

Here let it be pointed out that associations are not always the result of experiences with the environment. Some are developed in imagination, as, for instance, when a child imagines that his mother will punish him for some act when actually she might be quite sympathetic. As a rule one's imagination conforms fairly closely to reality, or else one realizes that his fantasy must not be made the basis of reasoning. Otherwise the organization in the mind tends to be less coherent. As years of experience pass, the individual's mind becomes more and more firmly organized. His sentiments, ideals, standards and beliefs become consistent guides to direct his behaviour; and, although always somewhat pliable to the effects of new experiences, the organization normally tends to assimilate such experiences rather than being disrupted by them.

(b) *Disorganization of the mind.*—In the hebephrenic type of schizophrenia this harmonious organization fails. Conflicting rather than consistent associations develop, particularly those of a sentimental nature. Both subconscious and environmental factors may influence this development. Repressed complexes may impel the individual to actions which he cannot harmonize with the standards of those around him. He finds it difficult to adjust his sense of values. Because he wishes something that is taboo he may hate himself at one time for his weakness,

and again he may hate his environment for the restrictions it imposes. Thus conflicting and unsatisfactory attitudes become associated with the same situation. Inconsistent conditions in his environment may add to this lack of organization. For instance, the sentiment of love for a parent may conflict with feelings of hate aroused by unhappy experiences with the same parent. Or the interest in school work may be offset by antagonism to real or imaginary unfairness of the teacher. The pupil may thus fail to develop a normal appreciation of the value of an education, and his life at school becomes dominated by inconsistent sentiments which lead to further unfortunate experiences.

This condition may be aggravated by imaginative processes. The individual may build up in his imagination new and unnatural associations. Introspection makes him even more confused. Because of the conflicting ideas in his mind he has no fixed standards by which to judge his problems. Standards to which he formerly adhered may be shattered by some new experience, leaving him more confused than ever. The systematic structure of his mind becomes disorganized, disintegrated and incoherent. One usually finds that such a patient has had strong emotional tendencies, but has had difficulty in sentimental adjustments. Ideas of affection, ambition, sex, religion, etc., may have been prominent but never satisfactory. The individual may have made strenuous attempts to face life, but with repeated failures. There is often a sensitive, introspective nature, with a feeling of inferiority. Due to the disorganization of the mind, symptoms of incoherence are prominent— incoherence of thought, incoherence of action, incoherence of emotion. The imaginative tendency has not diminished, and hallucinations and delusions are prone to develop. Also, there need be no diminution of energy but a continued effort to combat difficulties with resulting outbursts of feeling or action. The disorganization being progressive, deterioration is usually rapid, and recovery unlikely.

(c) *Example of hebephrenic type.*

(Case No. 5906 P.M.H.).—This girl was admitted on November 16, 1932, at the age of 21. Her father is reported to have been alcoholic and shiftless, and to have deserted the family before the patient was born. At birth the patient weighed three pounds, and she was not robust until in her "teens". Her early development was otherwise normal. She made good progress in school to Grade VII. Then she took three years to get through Grade VIII. She stated she had a poor teacher

and "didn't know what it was all about". She spent two years in Grado IX; she was afraid of herself and felt she could not cooperate with the teacher; she would try to memorize the textbooks. She did better in Grade X, and finally passed most of Grade XI at the age of 20. In the final year she had a good teacher, but she regarded him as her enemy because he was sarcastic and he thought she would not pass; she worked hard to show him that she could.

Up to this time she had lived at home. Her mother, to whom she was greatly attached, died when she was 17, but the patient continued living with her brothers. Although she earned some money in a telephone office she gave that to her brothers. They did not treat her considerately. If she wanted some money she might have a quarter tossed across the table at her. She said she loved one brother, although he criticized her. The other brother, she said, was inhuman. She apparently felt out of place at home and that she was practically told to get out in the end. At the age of 20 she obtained a position away from home. Her work was satisfactory, but she was not altogether happy. Her effort was chiefly to show people that she could succeed. She did not feel at one with her companions, and said she should have given them a piece of her mind and they would have thought more of her. She felt that they "picked" on her. At the end of one year she suddenly broke down and her present illness became manifest.

Before her illness she was considered lively and fond of company, and nearly always happy and placid. She was sensitive. Sometimes she was over enthusiastic and energetic. She had a marked feeling of inferiority. She showed no real self-criticism but a great deal of self-defense. She struggled to succeed, not for the benefit she obtained but to show people she could do it. She felt misunderstood and appeared unable to interpret other people's personalities properly. For instance, she said of one of the girls who tended to be rather abrupt, "I suppose she was trying to show her dirty disposition". She said of another girl, how selfish and how brainy she was, and yet how she liked her. She was surprised that the girls with whom she mixed could say such harsh things. She seemed to have envied other girls who had more excitement, and yet she was outwardly intolerant of undue familiarity or sexual laxness. She admitted having gone to rather wild parties which did not appeal to her, but she went to try to be like other people. After such affairs she would feel disappointed and disgusted with herself. She smoked heavily at times, and occasionally took liquor. She practised masturbation, and had at least one heterosexual experience. At the age of 18 she suffered from goitre and had a nervous breakdown.

Her present illness probably developed insidiously. It would appear that for years she had difficulty in forming her ideals and standards and her opinions of other people and her relations with them. She was harassed by conflicting ideas and obtained no help from others in adjusting them. Her symptoms became manifest suddenly at the age of 21. She became excited and noisy. She had ideas that people were trying to kill her. She said she had a master mind, and expressed other strange ideas about youth and people trying to kill youth. She addressed remarks to God and to people at a distance. Emotionally, she was very changeable, laughing, crying, fearful, euphoric. She showed flight of ideas and some incoherence. She would be concerned about trivialities. For instance she said she was contradicting Shakespeare. He wrote a ballad to Lady Eyebrow, but "You could not write a long ballad to any eyebrow, it is such a small thing, especially when plucked as girls have them these days". She spoke freely of sexual matters.

This patient's condition has become progressively worse. She is extremely hallucinated, violent, destructive, noisy, silly, dirty, profane and vulgar. Her speech is usually quite incoherent, but indicative of bizarre changeable delusions. She has spoken of her hands as being "strangler's hands", "the devil's hands", etc.

She was emotional, tense, and energetic. One always had the feeling that there was something pathetic about her, that she struggled to make good, only to find her mind becoming more and more confused with conflicting ideas until it disintegrated into a jumble of rebellious thoughts.

PART III.

CATATONIC TYPE OF SCHIZOPHRENIA-INTERPRETED AS A DETACHMENT FROM REALITY

(a) *Normal attachment to reality.*—Early in his development a child begins to recognize that things about him are real. At first his contact with an object produces only uninterpreted sensations. Gradually sensations begin to have meaning for him. He finds that they are caused by certain things. He learns that these things are concrete; they are real; they exist in a certain position, perhaps at a distance from him; they have meaning; he can expect certain experiences with them. Thus his sensations are no longer uninterpreted, they are elaborated into percepts. He develops a recognition of the concrete world of which he forms a part. He also develops a relationship to this world, a rapport, a condition which keeps him *in contact with reality*. Although one rarely analyzes this relationship, there is in the normal mind no tendency to doubt the reality of the environment. For instance, when awake, one does not normally have any feeling that he is in a dream. There is, however, another form of experience which he must learn to distinguish. He may recall in memory incidents which have occurred in the past. Similarly, he may produce in imagination situations which he never experienced in reality. Nevertheless, he distinguishes between the objective facts of his environment and these imaginative ideas and memories which may come into his mind.

At the same time he learns to utilize his imagination. Ideas may be allowed to run freely in a wish-fulfilling way, as in fantasy; or they may be directed in a constructive way to develop a theory, or solve a problem, or produce a story, or anticipate an interview, or plan a trip, etc. Such imaginings may in many cases excite one's emotions much as the real experiences would. Witness, for example, the erotic excitement caused by voluptuous fantasy, or the tears or laughter produced by reading fiction. Normally, however, one retains his awareness that these experiences are not real and he rarely reacts to them with overt activity.

(b) *Detachment from reality.*—In the catatonic type of schizophrenia the patient ceases to distinguish between what is real and what is imaginary. He loses his rapport with his environment. His focus of consciousness becomes detached from reality and centred chiefly upon his imaginative preoccupations. In this type the personality is not disorganized as in the hebephrenic, but its organization has progressed in more or less opposition to the environment. Many of these patients are of a determined disposition, prone to accept their own views in defiance of the doctrines of others. Some of them are imaginative and dreamy and inclined to indulge in fantasy. Their subconscious impulses are harmonious within themselves and in keeping with their imaginings. That is, an organization has developed in the patient's mind distinct from his overt activity. He recognizes, while normal, the scheme of things in reality, but he also has a scheme of things of his own.

Frequently the onset of the symptoms is sudden, although it is sometimes gradual. The patient ceases to distinguish between the reality around him and the ideas which occur in his imagination directed by his subconscious. His view of his surroundings becomes fogged, and his sense impressions are interpreted in terms of his imaginative preoccupations. He may completely withdraw from reality and go into a stupor, or he may react to his surroundings in a disordered way, guided by his fancies. Many such patients admit that they feel as if in a dream and that their surroundings seem unnatural and sometimes peculiarly altered. The freedom with which imagination acts in this type leads either to vivid fantasies or to actual delusions and hallucinations. These are frequently wish-fulfilling in nature, but distressing, self-accusatory, or paranoid ideas may occur. Owing to the fact that the fabric of this psychosis develops in the imagination and is detached from reality it remains possible for the patient to return to reality and see it again clearly and normally. This accounts for the fact that a proportion of these patients recover. There need be no disorganization and no distortion of reality as in the next type.

(c) *Example of catatonic type.*

(Case No. 6327 P.M.H.).—This patient was a young man of 26 at the time of admission on November 7, 1933. His family history was negative.

His personal history was normal up to the age of 16 when he had an attack of poliomyelitis which left

him with a partial paralysis of the right leg causing a pronounced limp. He stayed at home and attended school at irregular intervals until shortly before admission. He was in Grade XII. His personality had changed considerably as a result of his physical disability. Formerly very fond of sports, he never became reconciled to the limitation of his activities. He became sensitive, independent, and seclusive. He was more imaginative, inclined to day-dream, and to brood over his condition. He became irritable and quarrelsome. He admitted masturbation but denied any interest in girls; he felt girls would not be interested in a cripple like him. At the age of 21 he had a so-called nervous breakdown.

Symptoms of his present illness became manifest in September, 1933. He became worried because he anticipated extra work at home besides his school work. He had to give up school and was unable to do anything at home. He felt dazed, and started to hear voices of girls talking about sex matters. After admission to hospital he was usually quiet and cooperative but had occasional impulsive outbursts. He was rather disinterested and chiefly concerned with the voices, which he said he enjoyed. He said they took the place of normal activities in which he could not participate.

The patient had good insight and gave an interesting description of his illness. Its genesis seems to go back to his attack of poliomyelitis ten years ago. His physical disability "killed his interest in sports and other things". He had nothing to keep his "mental vitality up" and he gradually declined. He felt as if people treated him differently. He lost interest in things he was doing and turned to things he imagined. He lived more in his own thoughts; "there was nothing else to do". He day-dreamed, wishing he could get out and do the things other people were doing. When his psychosis became manifest he felt dazed. "It was a sort of sinking feeling, like going down in an elevator with no bottom. It could only be mental because things were still the same". He felt "separated from people, out of touch with them". Friendships and everything had changed. People seemed far away. The world seemed different, but he knew that it was only he who had changed. Sometimes people's remarks seemed to have a meaning out of the ordinary. He was worried because he could not understand things. "I didn't know where I was at." It is interesting to note that when he was more closely in touch with reality, as when he was doing occupational work, he found the voices much less noticeable.

PART IV.

PARANOID TYPE OF SCHIZOPHRENIA INTERPRETED AS A DISTORTION OF REALITY

(a) *Normal view of reality.*—It is not only necessary that the normal individual should be in contact with reality but also that his view of reality should be clear and accurate. This depends on judgment. Just as the normal lens of the eye focuses innumerable rays of light on the retina, to form a clear picture of the spacial relations of objects, so also normal judgment presents to the mind a clear picture of the relationship of objects and situations in life. Strictly speaking, judgment is based on experience; one recognizes the significance of a situation today because he associates it with similar situations he has experienced in the past. Most

frequently these associations act unconsciously, and one is quite unaware of why he forms a certain opinion. For example, he decides that he likes a certain individual (on the basis of past experiences with him or with others like him) although he is unaware of why he is so attracted. A higher form of judgment is involved when there is conscious reasoning upon which a decision is based. In all cases, however, the accuracy of one's view depends on the appropriateness of the associations which are utilized (consciously or unconsciously).

Certain factors may influence the associations which are utilized, and therefore affect the conclusion drawn. Some prejudice or the mood of the moment may obstruct the natural associations and cause the individual to react to quite inappropriate associations. For example, a teacher who has just had a quarrel with a colleague may see only the faults in her pupils' work and be blind to the good qualities. Or a strong Conservative may criticize some Liberal for discharging an employee, although the Conservative knows nothing about the circumstances; his judgment is based on quite inappropriate associations, *viz.*, the other is a Liberal and therefore wrong. Similarly, subconscious forces may have a profound influence on one's judgment. The man who has repressed a feeling of guilt for some misconduct may consequently be the first to condemn his fellow man for the same offense—his own feeling of guilt is associated with the other man's misconduct and forms the chief basis of his judgment. Thus it happens that, contrary to the logical process, one frequently makes a decision first on the basis of unrecognized associations and then proceeds to justify the decision with plausible explanations. This is the process of rationalization.

Opinions once formed tend to be a basis for future opinions. This is the process involved in learning as well as in many every-day judgments. We think, for instance, that if a man is once a thief he is always a thief, and we judge him accordingly. Erroneous judgments as well as accurate judgments tend to be perpetuated in this way—the reputation of the supposed thief may be false from the beginning. A normal person, however, is usually sufficiently adaptable that his view of important matters is harmonious with the realities of life as he is exposed to them. That is, he has a sufficiently accurate view of his environment to be able to react to it in a satis-

factory manner. His knowledge and beliefs, though not infallible, are compatible with the views of those around him.

(b) *Distortion of reality.*—In the paranoid individual, however, this does not occur. Such an individual is usually energetic and observant of things about him, particularly the actions of others, but he is prone to jump to conclusions and put his own interpretation on things. His judgments are biased. He does not give others the benefit of the doubt.

Due perhaps to repressed wishes or to his own inability to achieve his ambitions, he may become dissatisfied with his circumstances in life. Although unaware of the real cause of this dissatisfaction he adopts a constant attitude of suspicion, self-defense and prejudice, which interferes with his proper view of life. His astigmatic judgment persistently presents situations in a distorted form. This causes him to put the blame on others and to see faults in them which he should see in himself. His distorted view is perpetuated and elaborated from one situation to another, and, due to a series of consistent misconceptions, he educates himself to an erroneous belief, a system of delusions. As his opinions become more and more out of harmony with his environments, so also his actions become disordered, and he reacts, not to his actual environment but to his distorted view of it. His interest and energy do not fade but they become restricted to the factors pertaining to his delusions, which absorb more and more of his attention. In some cases the patient maintains close contact with reality, and limits his imagination to creating false interpretations, affected by his prejudice, but otherwise logical. Such cases may come in the class of true paranoia. If, however, he allows his imagination freer play and accepts poorer judgments which are more obviously wrong, he will come in the class of paranoid schizophrenia. Although such patients do not become detached from reality they accept more imaginative ideas, their delusions are far fetched and perhaps extremely grandiose, and hallucinations are prone to develop. In all paranoid cases the individual's view of reality goes through a steady process of distortion based on illogical deductions, so that it is almost impossible for him to be re-educated to see the world normally. Moreover his view could only be corrected if his abiding prejudice could be overcome and this is almost impossible.

Therefore, the prognosis for recovery is bad. On the other hand, in as much as the minds of such persons do not become disorganized, and their interests and energy are fairly well maintained, there is less tendency to deterioration.

(c) *Example of paranoid type.*

(Case No. 5934 P.M.H.).—This man was 46 years old when admitted on December 6, 1932. There was no history of nervous or mental disease in his family. He was born in Scotland. His infancy and childhood were normal. After finishing the second year in high school he worked in an accountant's office for a while. In 1904 he came to Canada. As he did not like farming he soon obtained work in a bank. He was overseas from 1915 to 1919, during which time he contracted gonorrhœa. Returning to Canada he held several positions as a bank manager. Being dissatisfied with this he eventually became a life-insurance agent.

He was always very reserved, shy, and suspicious. He was ambitious and serious-minded. He was only slightly interested in women. "The feeling I have had about my infection has deterred me from seeking female associates". He had a history of diphtheria, pleurisy, trench fever and gonorrhœa. There were no previous mental illnesses.

Although his present illness became manifest rather suddenly, its etiology may be traced back through many years of misinterpretation of his environment. While in the bank before the war the patient repeatedly thought that he was not getting the promotion he deserved. In 1910 he "believed favouritism was being shown". His salary increases were small, yet he thought he did more than his share of work. "It took three junior men to replace me." He was suspicious of one of his seniors and had friction with him. "He did not see things as I did. I tried to keep things straight. He was not treating the bank the way he should have done." During his military career he qualified as a captain, but was never given an appointment. He felt his senior officers discriminated against him because he stood up for the men. When in the position of bank manager he clashed with an inspector. "He practically called me a liar about statements of fact. It was probably foolish of me to lose my temper. He reported that I had a peculiar disposition and was unfit to be a manager where there was competition." In the insurance business he was not as successful as he antici-

pated. He therefore developed the idea that his prospect list was being tampered with. He felt superior to his manager and was suspicious. He imagined the manager was afraid he would get his job.

About this time the patient imagined an old military companion was spreading the tale that he had syphilis. He thought others talked about him and that they shunned him. He believed they gave him dope to increase his sexual feelings. He became interested in a girl, thought he heard her voice, and became jealous of another friend of hers. When committed to hospital he thought he had been framed. Since then he has got steadily worse. He has been suspicious, fault-finding, uncooperative and abusive. He hears obscene voices and feels that he is being worked on with electric rays. His speech is coherent and there has been little deterioration.

CONCLUSION

Although these four psychologically distinct processes may be distinguished (diminution, disorganization, detachment, and distortion) and a few patients display them typically, one finds that most schizophrenics do not fit distinctly into any one group. This appears to be due to the fact that frequently several of these processes are going on in one individual with the result that the manifestations are mixed. Rather than to classify each case as belonging to one particular type of schizophrenia, it might be better to estimate which is the predominating process involved and what proportion of the other reactions may be present. Diagnosis would thus be interpretive rather than symptomatic, and the prognosis as to recovery, arrest, or deterioration, would be rational rather than categorical.

The writer wishes to express his thanks for the assistance of Dr. G. A. Davidson, Superintendent of the Provincial Mental Hospital, at Ponoka, Alberta, and his permission to refer to hospital cases.

AMPUTATION OF A LIMB UNDER LOCAL ANÆSTHESIA.

—L. Dambrin considers that general anæsthesia for the amputation of a limb is often followed by grave post-operative complications. The patient may be severely injured and in a state of shock, or suffering from an acute infection or gangrene, and the administration of general anæsthesia is liable to lead to complications in the liver, heart, or lung. Local anæsthesia is most satisfactory, and ensures an amputation without operative mortality or complications. A method is described by which complete anæsthesia of the arm can be obtained in three minutes and of the thigh in four minutes. The only case in which this form of anæsthesia is stated to be unsuitable is that of the amputation of the thigh of a fat woman. The method which has proved the most successful is the circular infiltration of the various layers of the limb, beginning with the skin, then the cellular

tissues, muscles, nerve trunks, down to the bone. A solution of 1 or 2 per cent novocain without adrenaline is injected after a tourniquet has been placed round the upper part of the limb. Three punctures are made in the arm and three or four in the leg, and the needle is rotated in each place. The amount of solution used is about 100 c.cm. for the arm and 150 c.cm. for the thigh. By this means perfect anæsthesia is obtained, and the amputation can be conducted without any risk of pain to the patient. In twenty cases reported there were no signs of intolerance to novocain, convalescence was uncomplicated, and there was no operative or post-operative death due to the anæsthetic. Since the series of cases included several patients suffering from diabetic gangrene or a virulent infection, it is pointed out that this would not have been the case had a general anæsthetic been given.—*Rev. de Chir.*, March, 1936, p. 245. Abs. in *Brit. M. J.*

MUSSEL POISONING IN NOVA SCOTIA

BY ARTHUR L. MURPHY,

Halifax, N.S.

THE old warning, never to eat shell fish in months without an *r*, probably originated among the folk who live by the sea, and had no more scientific basis than the belief that good sauerkraut can be pickled only in the full of the moon. The superstition about the sauerkraut has been pretty well discarded by the younger generation in Nova Scotia, but those who enjoy the relish claim that it is not so good as it used to be. Disregard of the shell fish warning has resulted more seriously. There have been two fatalities, attributed to the eating of mussels.

On July 7, 1936, at 1 p.m., Dr. F. E. Rice, of Sandy Cove, Digby County, was called to Centreville, some five miles distant, to a sick boy. Responding immediately he found a well developed boy of eight years, deeply unconscious. His colour was very pale; he was pulseless. The heart could just be heard, being very rapid and weak. Within ten minutes he was dead.

The patient, with another boy of his own age, had gone to the shore in the morning to gather mussels. Centreville is on St. Mary's Bay, an inlet of the Bay of Fundy, and the blue-black shell fish are to be found in abundance on the mud flats when the great Fundy tide has swept out. At about 10 a.m. they cooked the mussels over a fire and ate an undetermined number. Shortly after, feeling ill, they went their own ways home. The patient vomited persistently and complained of faintness, but it was not until this merged into coma that his father became alarmed and called the doctor. The boy's companion, after a bout of vomiting and vertigo, made a rapid recovery.

At 1.30 p.m., the same day, Dr. Rice was called to East Ferry, fifteen miles from Centreville. He found two men faint and vomiting. They complained of numbness in their hands. Lying on the floor was a third, deeply comatose, moribund. His pulse was 160; his hands were pressed against his abdomen. In fifteen minutes, two hours and a half after eating mussels, he died. His companions quickly recovered. They had eaten only a few mussels, both cooked and

raw, whereas the victim had taken a considerable number. Dr. Rice regretted that the rapid termination of both cases made a more complete clinical picture impossible.

Shell fish poisoning has been recognized as a clinical entity for over a century in Europe where it was first described and the literature records 120 cases with 24 deaths. Outbreaks in California during the past nine years have produced 240 cases with 14 deaths and the only thorough work done on the problem comes from the University of California. Hermann Sommer and Karl F. Meyer of the George Williams Hooper Foundation have done extensive research (*Calif. & West. Med.*, 1935, 42: 423) and, while the exact nature of the poison has not been determined, valuable facts have been established.

The poison is most common in the mussel but has been found in the clam and sand crab. Guinea pigs fed on a species of clam gathered on the Bay of Fundy shore in the regions of Centreville and East Ferry died in forty-five minutes. Their brethren, fed on mussels from the same areas, died after a longer interval. Like the human beings, some of the guinea pigs escaped after a slight illness or none at all. Beyond confirming the presence of the poison no experimental work was done at the provincial laboratory at Halifax, specimens being shipped to Dr. Meyer in California. Nevertheless a few observations may be drawn from the local cases which conform with the established findings.

First, the poisoning takes a paralytic form. Although no information could be elicited from the fatal cases the two men who recovered complained of numbness in the hands. This may extend from the four extremities until the whole body is paralyzed. The poison is quickly eliminated; the recoveries of those who escaped death were rapid. It is present in fresh mussels. It is not present in lethal quantities in all the mussels of a particular region, nor are the mussels of any region always poisonous. Many have eaten of St. Mary's Bay shell fish without ill effect. The poison is not from contaminated

water. The Bay is too exposed to the Atlantic, its shores too sparsely settled, to make this tenable. The poison is not destroyed by boiling or cooking, or the boy would not have died. From the rapidity of its action it is not likely bacterial, and cultures made from different parts of the mussels confirm this.

Meyer and his co-workers, gathering mussels near San Francisco over a seven-year period, and determining the degree of toxicity by the intraperitoneal injection of mice, have shown the almost constant presence of poison. This is highest in the summer months, from June to September. In some years this peak transcends the lethal danger line, in others it does not. The occurrence of poisoning cases has been found to coincide with these results.

Mussels gathered at the lowest possible level are more poisonous than those exposed to the sun or those gathered in placid, land-locked bays. This suggests that the source of the poison may be in the sea, possibly the plankton on which the mussel feeds. Experiments in this direction have not been conclusive.

The poison is a basic alkaloid. The purest preparations so far obtained are lethal to mice in doses approaching one-millionth of a gram on intra-peritoneal injection. Thus it may be present in sufficient amount to kill without outward warning of its existence. It is one of the most active known of rapid poisons. Only the antigenic toxins of some plants and bacteria are more potent. It is present in the digestive gland and the fluid about the fish. The muscle is probably unaffected.

The basic molecule has no distinguishing feature, although, usually, it has a fuller intestinal tract and larger digestive glands than its normal state. There is no known antidote to the poison. Eighty per cent may be neutralized by boiling in soda bicarbonate solution for twenty minutes. Here, unfortunately, cook and toxicologist disagree. Education of the people would seem to be the only safeguard, and they have been warned not to eat mussels in the months without, September and October being added, if only to show that science really is greater than superstition.

CARBON TETRACHLORIDE POISONING*

BY CECIL YOUNG, B.A., M.B.(TOR.), M.R.C.P.(LOND.),

Toronto

CARBON tetrachloride, used as a solvent for fats and oils, has been in common use in industry and in the home for many years. The safety element has been stressed, because it is non-inflammable as compared with gasoline and similar dry-cleaning preparations. Carbon tetrachloride is also an ingredient of "Pyrene" or similar hand fire extinguishers in common use in buildings, yachts and motor cars. As a vermifuge it has been used internally in the treatment of hookworm disease.

Recently it has been noted by many observers that carbon tetrachloride is not without danger if the fumes are inhaled in concentration. Butsch¹ reported poisoning in a workman who used carbon tetrachloride in cleaning old telephones. McGuire² reports seven cases of poisoning in employees of a dry-cleaning establishment where carbon tetrachloride was used. Alice

Hamilton³ notes the danger of carbon tetrachloride as a fire extinguisher in the presence of heat in a closed space, under which conditions phosgene is generated. The *New York Times*, July 7, 1932, reported a fire in a New York subway in which "Pyrene" fire extinguishers were used and 150 persons were overcome with the fumes, which were probably a mixture of carbon tetrachloride, phosgene, and chlorine. The *Journal of the American Medical Association*,⁴ in an editorial on the subject, states that in Portsmouth Navy Yard in 1919 two men died from the fumes produced when the clothing of one caught fire and Pyrene was used to extinguish the flames. The same editorial also reports poisoning from carbon tetrachloride used in Switzerland as a solvent for floor wax.

McMahon and Weiss⁵ were of the opinion that an individual's susceptibility played an important part in tetrachloride poisoning, and also stated that patients who were accustomed to the

* Read before the Section of Medicine, Academy of Medicine, Toronto, February 11, 1936.

regular consumption of alcohol were particularly susceptible. They concluded that the sensitivity was increased not only because of the increased absorption of the drug and the synergistic action of the alcohol and carbon tetrachloride but also because of the possible existence of pre-existing liver damage in alcoholics.

The majority of cases reported have shown liver damage due to central necrosis, and a few cases have been reported as exhibiting kidney damage, including that of Lehnher⁶ who made a very complete study of the blood chemical changes on an alcoholic patient who drank four or five ounces of carbon tetrachloride. The case I am about to report differs slightly in that the patient was practically a total abstainer from alcoholic drinks, and received practically no liver damage but severe kidney damage, the latter to such an extent that on noticing the blood chemistry figures one is gratified at the remarkable and steady improvement following intravenous therapy.

CASE REPORT

Mr. H. B., aged 42, married, embalmer, was admitted to the Toronto Western Hospital on October 29, 1935. He stated that he had been in good health until ten days previously, when he had carried out an extensive fumigation, lasting two hours, in a small room with the doors and windows closed, by spraying walls, floor and baseboards with a liquid obtained from a neighbour who worked for a fire extinguisher manufacturing company. The substance was found to be carbon tetrachloride. That evening, about an hour after he finished fumigating, he experienced cramps in the upper abdomen, with extreme fatigue, nausea and vomiting. The nausea and vomiting had continued at intervals up to the time of admission, with obstinate constipation, and during the past two or three days he had passed very little urine and his vision had begun to blur. He mentioned that his wife and two children had felt nauseated the evening of the fumigation, but had felt perfectly well since.

Personal history.—He had had rheumatic fever; tonsillectomy three years ago. He was a moderate smoker and practically an abstainer from alcohol.

Family history.—Irrelevant.

Physical examination.—The man appeared ill; his expression was strained and pallor marked. His pupils were equal and reacted to light and accommodation; ocular fundi normal. Some blurring of vision was noted. Hearing was normal. Post-nasal discharge; tongue heavily coated; lower teeth, carious. There was no enlargement of cervical or other glands. The thyroid was not enlarged.

Cardiovascular system.—Pulse 85; no radial sclerosis. Blood pressure, 160/84. The heart was slightly enlarged (apex 9.5 cm. to left, in fifth space). Heart sounds clear and of good quality.

Lungs.—Normal.

Abdomen.—Some vague tenderness in right upper quadrant and posteriorly over right costo-vertebral angle.

Nervous system.—Involuntary twitching of hands. The tendon reflexes were all a trifle exaggerated. Babinski and Kernig signs were not elicited.

Urinalysis.—Urine, alkaline; specific gravity, 1.017; albumin, 2 plus; sugar, negative. Microscopically, red

blood cells, 30-60; white blood cells, 200-250; a few granular casts; mucus, 2 plus.

Blood count.—Red blood cells, 4,700,000; white blood cells, 9,300; haemoglobin, 70 per cent. Differential count.—Neutrophils, 72 per cent; eosinophils, 2 per cent; lymphocytes, 23 per cent; monocytes, 1 per cent.

Blood Wassermann test.—Negative.

Blood chemistry.—Non-protein nitrogen, 203 mg. per 100 c.c.; creatinine, 22.7 mg. per 100 c.c.; van den Bergh, very slightly biphasic; icterus index, 9.

Blood culture.—No growth.

Blood grouping.—Type 1 Jansky.

November 6, 1935, galactose tolerance test.—40 g. galactose.

Hour	Quantity	Galactose
Fasting urine	150 c.c.	negative
2 hour	138 c.c.	very strong trace
5 "	225 c.c.	negative

Diagnosis.—Carbon tetrachloride poisoning; acute nephritis and uraemia.

Treatment.—Intravenous glucose, 25 per cent, 300 c.c., was given twice a day; calcium gluconate, 10 per cent, 10 c.c. intravenously, twice a day. Diet: fruit juices and glucose drinks only.

Progress.—The patient commenced to improve at once after the use of intravenous glucose and did not vomit after the third day, but on the fifth day an exsanguination transfusion was done, removing 800 c.c. of blood and replacing it with 500 c.c. of donor's blood with the addition of 1,000 c.c. of 5 per cent glucose. This apparently was of great benefit to him. On the seventh day his diet was changed to one consisting of banana, 900 g.; cream, 200 c.c.; cream soup, 200 c.c.; milk, 200 c.c.; and cocoa, 200 c.c., giving him a value of 1,585 calories and a protein content of 35.4 g. By the ninth day the urine had improved so that there was only a slight trace of albumin, and microscopic examination showed only an occasional pus cell with no red blood cells or casts, although from the amount of glucose given intravenously he showed an occasional trace of sugar. The level of non-protein nitrogen and creatinine in the blood showed a steady decline, and his blurring of vision had cleared by the sixth day. At no time did he show any further evidence of hepatic derangement other than a faintly indirect van den Bergh reaction and an icterus index of 9. He made an uninterrupted recovery. The blood chemistry figures are interesting.

Date	Non-protein nitrogen in mg. per 100 c.c.	Creatinine in mg per 100 c.c.	Diet
Oct. 31st	203	22.7	Fruit juices and glucose.
Nov. 1st	207		
Nov. 3rd	203		
Nov. 4th	179		
Nov. 5th	160		Nov. 6th
Nov. 6th	140		Protein, 35.4 g.
Nov. 7th	112	8.9	Calories, 1,585.
Nov. 8th	98		
Nov. 9th	77		
Nov. 10th	72		
Nov. 11th	63		
Nov. 12th	54		
Nov. 14th	56	2.6	Nov. 15th
Nov. 15th	46		C.300 P.30 F.40
Nov. 20th	42		Calories, 1,680.
Nov. 21st	39		
Nov. 23rd	35		
Nov. 27th	35	1.7	Intravenous glucose and calcium discontinued.
Dec. 8th (after 26 discharge)			

COMMENT

This case illustrates the profound and rapid toxic effect of the inhalation of carbon tetrachloride fumes on the kidney, and also illustrates the value of glucose and calcium intravenously in this condition. The subjective symptoms improved dramatically after the exsanguination transfusion, and I believe this to be a useful procedure in such cases. For the use of calcium we are indebted to Minot and Cutler* who found that dogs poisoned with carbon tetrachloride could be treated with injections of calcium, also

that with a high calcium diet dogs were relatively immune.

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OBSERVATIONS ON THE INTESTINAL FLORA FOUND IN MONTREAL

BY PAULINE BEREGOFF-GILLOW, Ph.G., N.S., M.D.,*

Montreal

OWING to the uncertainty prevailing regarding the distribution and significance of parasites and pathogenic bacteria of the intestinal tract, and due to the general lack of knowledge about the etiology of certain intestinal diseases, the slightest observations may have some degree of value in promoting further research. I present, therefore, some data on the intestinal flora, both bacterial and parasitic, which I have obtained from a study of 400 cases.†

MATERIAL

Repeated specimens of feces were examined from the following persons (in the majority of cases as many as 10 to 12 specimens):—

Children....	200	Hospitalized for different causes (heart, lungs, tonsils, etc.).
	25	With history of gastrointestinal upsets (diarrhoea, cramps).
Infants.....	3	Acute enteritis.
Adults.....	80	Ward patients with no apparent gastrointestinal disturbances.
	8	Ward patients with gastrointestinal upsets (diarrhoea).
	4	Ward patients; typhoid cases.
	25	Referred private patients with history of repeated diarrhoeas.
	55	Controls, from among the hospital staff (doctors, nurses, maids, etc.).

TECHNIQUE

All the specimens were obtained in as fresh a condition as possible, and examined as follows:—

1. Grossly—for adult worms.

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†The majority of cases were from the Women's General Hospital; several from the Montreal General Western Division; and 18 from the Montreal Children's Hospital.

2. Fresh cover-glass preparations—for ova, larvæ, amœbæ, etc.

3. Sediments—Rivas' concentration method¹—for parasites, encysted amœbæ, etc.

4. Cultures—Each specimen was plated directly on Endo and McConkey media. Those colonies differing from the *B. coli* type were transferred to standard agar plates and Russel stabs. If the cultures appeared pure after 24 to 48 hours' growth several colonies were then transferred to agar tubes and subsequently inoculated into dextrose, lactose, saccharose, peptone, gelatine, maltose and mannite broths, etc., for preliminary identification. Mixed cultures were separated by plating. All strains that seemed to show any characteristics of the paratyphoid, typho-dysentery, and Morgan groups were kept for further study. The majority of the strains transplanted and then discarded were those of the proteus type, *B. alkaligenes*, and those that slowly ferment lactose.

RESULTS

1. Intestinal parasites isolated:—

	METAZOA	
	Adults	Children
Cestoda—		
<i>Dibothriocephalus latus</i>	2	1
<i>Tania solium</i>	1	0
<i>Tania saginata</i>	0	1
Nematoda—		
<i>Oxyurus vermicularis</i>	0	21
<i>Trichocephalus</i>	3	10
<i>Ascaris Lumbricoides</i>	3	8

PROTOZOA		
	Adult	Children
Sarcodina—		
<i>Entamoeba histolytica</i>	12	0
<i>Entamoeba coli</i>	15	20
<i>Entamoeba nana</i>	5	7
Mastigophora—		
<i>Lamblia intestinalis</i>	5	20
<i>Cercomonas hominis</i>	2	4
<i>Trichomonas intestinalis</i>	2	7

Ciliata—

<i>Balantidium coli</i>	1	0
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Eleven of the children were infested with 2 or 3 species of parasites.

2. Bacterial pathogens isolated:—

Adults Children

<i>B. typhosus</i> ...	6	0	Of these, two were carriers. In one of the stools of a typhoid patient <i>E. histolytica</i> was also found.
<i>B. paratyphosus</i> "A"	10	0	Isolated from 5 cases of mild hyperexia with slight diarrhoea; from one attendant, considered the carrier, and from other 4 members of the staff who had no symptoms whatever.
<i>B. paratyphosus</i> "B"	4	0	These patients presented no gastrointestinal disturbances.
<i>B. artrycke</i> ...	3	0	These patients suffered from occasional diarrhoea, alternating with constipation. This organism isolated fermented dextrose, maltose, xylose, sorbitol, arabinose, dulcitol and trehalose. It produced H ₂ S, no indol, did not liquefy gelatine, and did not ferment salicin, lactose or saccharose.
<i>B. flexneri</i> ...	2	0	Normal persons.
<i>B. morgani</i> ...	2	3	The children had frequent attacks of diarrhoea; the adults, acute diarrhoea. Because of the fact that repeated examinations showed no other pathogens, and because the Morgan organism was constantly present, almost in pure culture, it is reasonable to believe that this organism was the etiological factor.

B. sonne..... 0 2

Both patients (infants) died of acute enteritis. This organism acidified dextrose, arabinose, maltose and manitol within 24 hours. Saccharose and lactose fermentation was delayed; the latter, 4 days; the former, 12 days. Dulcitol, sorbitol and salicin were not acidified. There was no liquefaction of gelatine, no indol, no H₂S. The bacillus was non-motile. It agglutinated Flexner serum 1:100; Sonne serum 1:100, and in no dilution with Shiga.

DISCUSSION

These observations indicate that systematic stool examinations would clear up a considerable number of unrecognized bacillary and parasitic intestinal infections which are the cause of, or may eventually lead to, gastrointestinal disturbances. They also stress the relative importance of recognizing the sources of these pathogens.

It is interesting to note that the children in these regions are harbouring the same type of flora as those of the tropics. Though there is a smaller percentage of infestations, the variety of the species is practically the same. Although we are inclined to believe that in these regions we are free from parasitic infestation and that our hygienic conditions tend to eliminate bacterial pathogens, I would, nevertheless, stress the desirability of an intensive study of the various types of gastroenteritis. I feel that a routine stool examination should have been generally adopted long before now, as is done in the tropics.

The epidemiological relation and the distribution of the types of bacterial and parasitic infestation deserve greater investigation, and more appropriate preventative measures should be taken.

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Case Reports

A CASE OF ANURIA LASTING TEN DAYS ASSOCIATED WITH MARKED TOXIC SYMPTOMS*

By A. S. SINCLAIR, M.D.,

Regina, Sask.

It is my purpose to present a case of anuria which lasted ten days and was followed by complete recovery. The anuria was preceded by partial urinary suppression for two days. Both the suppression and anuria followed a hæmolytic blood transfusion given to a patient subject to acute influenzal infection complicated by severe gastric hæmorrhage. The anuria was accompanied by marked symptoms of intolerance to the unexcreted poisonous nitrogenous substances in the blood stream. This patient had a solitary kidney; the other one was tuberculous and was removed in 1932.

During the period of anuria the following features were observed. (1) The blood clotted very rapidly. (2) The fragility of the erythrocytes was unusually increased. (3) The skin and subcutaneous tissue of the whole of the abdominal wall were riddled with deep-seated and extensive purulent lesions. These lesions resembled carbuncles. (4) The blood donor and recipient were cross-typed and said to be entirely compatible, and yet the transfusion was followed by delayed reaction.

CASE REPORT

The patient was a female, aged 32, with a history of catarrh of the upper respiratory tract, sneezing, and a non-productive hard cough, for 14 days. She had headache and epigastric pain for seven days, and a moderate fever for one or two days. The pain in the head, eyeballs and back was intense. Her vision was blurred and she complained of flashes of light in front of her eyes. She had vomited several times. The pain in her left lumbar region was particularly noticeable on the day of her admittance to the hospital, October 28, 1932. She also complained of some slight burning during micturition, shortness of breath, feeling of weakness and loss of appetite. Her bowels were regular and there was no frequency of urination.

Past history.—Appendectomy in April, 1930. Dilatation and curettage, followed by blood transfusion in November, 1930. The hæmorrhage was caused by an abortion of a four months' pregnancy. In December, 1931, she was confined to the Regina General Hospital for toxæmia of pregnancy. She was under my care and made an uneventful recovery. Later her condition was

found to be a right cornuate pregnancy and she aborted in March, 1932.

Nephrectomy was performed by Dr. Dakin and myself in April, 1932. We removed her right kidney which was practically destroyed by tuberculous infection. She was sent to the Fort Qu'Appelle Sanitarium for a rest cure for two and one-half months. She had been enjoying comparatively good health until her present illness set in. The family history was irrelevant.

Physical examination.—On admission the patient was toxic but ambulatory. She was thin, pale, and sickly looking. Her skin was dry, her pupils were sluggish, her conjunctivæ were injected, and photophobia was present. Her temperature was 104° F.; the pulse rate 98; respiratory rate 20; and the blood pressure 115/80. The lungs were negative except for some dullness at the bases on percussion. The apex of the heart was localized in the nipple line and there was a mitral systolic murmur. The pulse was dicrotic and somewhat irregular in character. There was definite tenderness and splinting in the epigastric region and over the left kidney region. The spleen was not palpable. The deep reflexes were sluggish. The remainder of the physical examination was essentially negative at this time.

Laboratory tests.—Red blood corpuscles, 3,328,000; white blood cells, 6,000; hæmoglobin, 68 per cent; colour index, 1. Urinalysis—urine was cloudy, of amber colour, acid reaction; specific gravity was 1.026; a faint trace of albumin; no sugar or acetone was present; an occasional pus cell and hyaline cast. The blood urea nitrogen was 28 mg. per 100 c.c. The blood creatinine was 1.2 mg. per 100 c.c.

Course.—October 27th to November 9th.—Septic temperature; severe headache, pain in chest and abdomen; face flushed and hot; drowsy; feeling chilly at times; slight epistaxis (once or twice), nauseated, belching up gas and vomiting undigested food.

October 31st.—No tubercle bacilli or pus found in urine.

November 14th to 19th.—Gradual rise in temperature, reached 104° F. on November 19th at 3 p.m. The same day she had a chill which lasted 20 minutes, and vomited. Face was flushed; eyes puffy, photophobia present; appetite is fair. Headache; complained of whistling sound in head; became very drowsy after the chill. Blood urea was estimated and reported to be 28 mg. per 100 c.c. Urinalysis, negative.

November 19.—X-ray of left kidney—left kidney outlined, inferior pole opposite the third lumbar vertebra. Kidney fairly low, slightly enlarged, no evidence of irregularity; psoas muscles normal; diaphragm normal.

November 20th to 24th.—Very drowsy, complaining of chilliness, vomiting, and perspiring freely. Slightly irrational.

November 24th.—Expelled 5 oz. of very dark red blood containing clots by bowel; the odour was very offensive.

November 25th.—Expelled 2½ oz. of very dark red blood containing clots; very offensive odour; patient very restless and pale.

November 26th.—Stool contained about 4 oz. dark red blood; involuntary micturition, very pale and restless; gave blood transfusion of 350 c.c. No immediate reaction. Two hours after arrival in ward developed chill lasting for 20 minutes. Stool contained 5 oz. dark clotted blood. Another bowel movement contained 2 oz. dark blood; patient appears tired and very pale, intake 32 oz., output 28 oz.

November 27th.—Pale, restless, vomiting, facial pallor pronounced, temperature subnormal, drowsy; gave intravenous saline; intake 22 oz., output 10 oz.; first indication of suppression of urine.

* Read before the Grey Nuns Medical Staff, Regina, May 28, 1936.

November 28th.—Appears brighter, temperature normal, no blood in stool, intake 33 oz., output $1\frac{1}{2}$ oz. Blood clotted with unusual rapidity. Fragility of erythrocytes was unusually increased.

November 29th.—Passed $\frac{1}{2}$ oz. of urine; very drowsy and restless. Cystoscopic examination by Dr. Dakin; bladder and ureteral opening normal; no obstruction to catheter; kidney irrigated with warm saline. Dr. Dakin obtained $\frac{1}{2}$ dram of urine from kidney and laboratory report was as follows: "From left kidney micro: few red cells ($1\frac{1}{3}$ h.p.f.), small round epithelial cells." X-ray of chest was taken. Heart is enlarged in the aortic and basal areas. Heart is centrally placed; enlargement is towards the right. Apices are clear. The film taken is a little light, showing rather intense lung markings with an indication of some mottling of the right chest, and passive congestion in the lower half of both right and left chest. One could judge from the appearance of the film that there is cardiac insufficiency producing basal lung stasis."

November 30th.—No urine passed; very restless, irrational, attempted to get out of bed, unable to obtain urine after catheterization; hands and feet trembling, vomiting.

December 1st.—Considerable twitching of limbs; lips very dry; very restless; hands cyanosed; unable to count pulse; spent a poor day.

December 2nd.—No urine obtained from bladder, several bowel movements, blood urea 220 mg. per 100 c.c. Creatinine 5.36 mg. per 100 c.c.

December 3rd to 8th.—Has not voided, developed deep skin sores all over her abdomen; very restless, trembling, mumbling. Nauseated; appears to have pain when she turns. Blood urea 260 mg.; creatinine 5.5 mg. per 100 c.c.

December 6th.—Hæmoglobin, 30 per cent; red cells, 1,880,000; colour index, 0.8. Differential count: white cells, 100; polymorphonuclears, 67; small lymphocytes, 33.

December 9th.—Frequent emesis of dark green fluid with bloody mucus. At 10 a.m. examination revealed distended bladder; catheterized and obtained 19 oz. of urine.

December 10th.—Brighter; voided 22 oz. Pustules on abdomen becoming larger.

December 11th.—Urine culture and examination for tubercle bacillus culture (after 11, 35, 48 hours) shows a pure culture of streptococcus; smear examination for tubercle bacillus was negative.

December 14th.—Blood urea, 296 mg. per 100 c.c.

December 24th.—Blood urea, 24 mg. per 100 c.c.

December 19th.—Phenolsulphonephthalein dye injected intramuscularly.

1st specimen....1.10 hour after injection 13 per cent (normal 40 to 50 per cent)

2nd specimen....2.10 hour after injection 10 per cent (normal 20 to 25 per cent)

3rd specimen....3.10 hour after injection 11 per cent (normal 20 to 25 per cent)

January 17th.—Phenolsulphonephthalein test.

1st specimen....15 minutes after injection 10 per cent

2nd specimen....30 minutes after injection 15 per cent

3rd specimen....60 minutes after injection 15 per cent

Total elimination of the dye.....40 per cent

39 to 40 per cent renal function slightly impaired.

January 29th.—The dye was injected intravenously.

1st specimen....15 minutes after injection 11 per cent

2nd specimen....30 minutes after injection 12 per cent

3rd specimen....60 minutes after injection 16 per cent

Total elimination of dye.....39 per cent

39 to 25 per cent is interpreted as renal function moderately impaired.

February 10th.—Report of gastro-intestinal tract. Stomach shows some spasm at pylorus; cap forms

normally on films; colon shows delay in emptying; evidence of slow motility, otherwise series is negative.

Urine: cloudy yellow, reaction acid; specific gravity 1.008; albumin negative; sugar negative; acetone negative, few leukocytes, epithelial cells.

February 11th.—Hæmoglobin, 63 per cent; red cells, 3,190,000; colour index, 1.0; white cells, 8,000; coagulation time, $3\frac{1}{4}$ minutes.

February 17th.—Colour, clear yellow; reaction neutral; specific gravity, 1.016; albumin, negative; sugar, negative; acetone, negative; epithelial cells microscopic.

December 24th to February 17th.—Slow urinary recovery; temperature ranged between 97 and 100 F.; pulse ranged between 80 and 100, excepting during chills, when it rose to 118. Respiration ranged between 20 and 40 per minute. Blood pressure ran from 88/52 to 106/70.

Diagnosis.—Influenza associated with gastric lavage, nervous and renal involvement followed by an after blood transfusion.

TREATMENT

Treatment must be by prophylactic method as little can be done, once suppression of urine has developed. The use of high titre sera tend to eliminate errors in grouping, while administration of fluids and alkalies before transfusion will ensure an alkaline diuresis, so any hæmolyzed blood will be excreted in urine. The following suggestions may be of value. (1) Hot applications or dry heat to kidney region. (2) Large amounts of fluid proctoclysis or hypodermoclysis. The addition of alkalis 2 per cent and of glucose 5 to 10 per cent. (3) Salt solution should never be used. (4) Decapsulation is of little value. (5) Section preceded by intravenous saline has been suggested if convulsions threaten. (6) Baths or sweats if cardiac condition permit.

COMMENT

Although the blood donor and recipient were cross-typed and said to be entirely compatible, this patient developed a *delayed blood fusion reaction*, confirming the idea that the agglutinin content of some donors' blood may be so surprisingly high, namely, instead of the usual 1:3, that serious reactions may ensue unless high titre sera are used in cross-typing the blood before transfusion.

On November 28th, when the laboratory technician obtained a specimen for a blood count, he found that the blood clotted very rapidly and would clot as soon as it was collected. This phenomenon was checked by Dr. Ho, Laboratory Director, and he stated that this was the clotting time unusually reduced by the fragility of the erythrocytes which was increased as well.

Two days after suppression set in this woman developed extensive and deeply-seated sores all over her abdomen. They were similar to multiple carbuncles of the skin. Over six weeks passed after the urinary secretion returned to normal before these cleared up. At present her abdomen is covered with irregular, healed scars.

In reviewing the literature, I have failed to find a case in which a patient with a solitary kidney and developing anuria with marked symptoms of intolerance to the poisonous nitrogenous substances for 12 days had survived. This patient recovered completely. Her kidney is functioning as well as it did prior to this illness. Her last urinalysis was done at my office a week ago and found normal.

One might venture to explain the recovery thus. Under normal conditions waste products are excreted by kidneys, liver, lungs, intestines and skin. The kidneys are of first importance. When they are unable to function the task may be assumed by the other excretory bodies. If the other excretory organs must do this work on short notice, as occurs in anuria, they fail to respond sufficiently to maintain life, because they have not been accustomed to act as substitutes. The reason this woman recovered may be due to the fact that she had a solitary kidney and the other excretory organs may have learned to substitute sufficiently to maintain life until the crisis subsided.

CONGENITAL ABSENCE OF THE CERVIX UTERI COMPLICATING PREGNANCY

By D. W. DAVIS AND J. F. HASZARD,

Kimberley, B.C.

A primipara, aged 26, first examined and diagnosed by Dr. W. Leonard, of Trail, B.C., was referred to us on her husband's transfer to Kimberley in September, 1935.

Heart, lungs and pelvic measurements were normal. There had been no previous operation, except for appendicitis. Pelvic examination revealed a shortened vagina and complete absence of the cervix uteri. The external os was very small.

It was decided to give her a test of labour before attempting more radical measures. Labour began about six p.m. on February 15, 1936, with intermittent light pains. Rectal ex-

amination at nine p.m. showed the head well advanced and no dilatation. At two-thirty a.m., February 16th, the pains became more severe and almost continuous. At four a.m. examination showed that the head was almost on the perineum with no sign of dilatation. As the os was obviously not going to dilate and we feared a rupture of the uterus, a Cæsarean section was done. With no cervix, a low Cæsarean was out of the question and the classical operation the only method possible. The further course of the case was uneventful, drainage through the small os being sufficient to allow a normal lochial discharge.

TWO CASES OF DIPHTHERIA OF THE CONJUNCTIVA*

By S. HANFORD MCKEE, B.A., M.D.,

Montreal

Fuchs distinguishes two forms of conjunctival diphtheria, namely, the superficial or croupous, and the deep (diphtheria of the conjunctiva in the narrower sense). The croupous form is characterized by the presence of a greyish white membrane which adheres closely to the surface of the conjunctiva, but which can usually be removed from it easily. The deep form runs a much more serious course than does the superficial, as in order for it to occur the exudate must coagulate while still within the tissues of the conjunctiva, so that the vessels are compressed and necrosis consequently occurs. The two forms described, which differ considerably in appearance and course, are due to the same cause, the Klebs-Loeffler bacillus. Often patients present other diphtherial patches, such as of the nostrils, angles of the mouth, or there may be a fully developed nasal or pharyngeal diphtheria.

CASE 1

L.O.N., a female of 9 years, had been in her usual good health until October 12th, 1934, when she fainted. She was put to bed and remained there the following day, as she complained of a general feeling of malaise. Her mother noticed that her left eye was red, but allowed the child to return to school the following day. She was brought to the eye clinic on October 19th. The left eye at this time showed a definite conjunctivitis, the lids were swollen, and over the palpebral conjunctiva of both lids a thin greyish membrane was seen, which could be removed by the platinum wire without bleeding. The membrane reformed rapidly, while a slide was being prepared for examination.

*From Departments of Ophthalmology and Pathology, Montreal General Hospital.

Read before the American Ophthalmological Society, Hot Springs, Va., on June 1st, 1936.

Examination of the smear showed micro-organisms morphologically similar to the diphtheria bacillus. Cultures were then made on Loeffler's blood serum, and organisms again morphologically similar to the diphtheria bacillus were found. The patient was transferred to the Alexandra Hospital for Contagious Diseases with a diagnosis of diphtherial conjunctivitis. During the course of her examination she had been taken to the Nose and Throat Department where examination showed no other evidence of diphtheria. The culture obtained was sent to the Department of Bacteriology of the McGill Medical School, and the report from Dr. F. Smith is as follows:—

"With regard to the micro-organisms in your case of diphtheritic conjunctivitis, I injected a guinea pig with the culture as it was received. There resulted only a slight local induration during the first few days. Metachromatic granules were not a prominent feature of the organism, and its fermentation reactions did not conform to those accepted for the diphtheria bacillus, so that my provisional report was that the organism resembled the Xerosis bacillus. On the fourth day the guinea pig died without any obvious lesion, and I repeated the virulence test with a larger dose of a young culture, giving a control pig 500 units of antitoxin. The pig died within 24 hours, a typical diphtheria death (local hemorrhagic oedema and hemorrhagic suprenals). After two days the control pig is perfectly well. Morphologically and biochemically, the organism would be missed, but there is no escaping the second guinea pig test. This is a diphtheria bacillus. It would be interesting to test its ability to produce toxin. I should not think that this is very high."

The patient received antitoxin treatment at the Alexandra Hospital, and was seen by me three days after her admission. Her eye had quieted very perceptibly and no sign of membrane was present. She made an uninterrupted recovery, and later (November 9th) was seen by me at the Montreal General Hospital, where the eye was found to be quite normal in every way.

CASE 2

M.D., a boy of 5 years, was brought to the Montreal General Hospital on May 27th, 1935, and when examined was found to have a well-marked membranous conjunctivitis of the right eye. Examination showed numerous organisms corresponding in morphology to the bacillus of diphtheria. A piece of the membrane was removed from the eye and sent to the Pathological Laboratory for investigation. Small fragments of the membrane were teased out upon slides and stained with old alkaline methylene blue and Albert's stain for *B. diphtheriae*. In the specimen numerous polymorphonuclear leucocytes and numerous straight and curved bacilli were seen. A good many of the bacilli showed clubbed ends and some of them segmentation. A specimen of the membrane stained with Albert's stain showed that the bacilli contained varying numbers of intracellular deeply staining granules. A series of tubes containing Loeffler's blood serum were inoculated with the membrane. There developed in the tubes over night one colony of *Staph. albus* and many colonies which contained in pure culture an organism which showed the characteristic morphology

and staining reaction of *B. diphtheriae*. After 40 hours' growth these colonies had increased in size, were sharply outlined, smooth and glistening, had a raised curve, and showed the typical poached-egg appearance of *B. diphtheriae*. When stained with old alkaline methylene blue and Albert's stain the organisms of which these colonies were composed showed the morphology and staining characteristics of *B. diphtheriae*. A typical colony planted in selected sugar serum waters gave the following reactions: Dextrose acid and no gas on dextrose, maltose and dextrin; no acid and no gas on saccharose, lactose and mannite.

Cultures of the diphtheria bacilli isolated, planted on Morgan's media (tellurite), showed black, discrete, shiny colonies with a grey margin.

In carrying out the virulence test, two guinea pigs of 240 gms. weight were used. On the day before inoculation one was given 500 units of anti-diphtheritic serum (Lederle). The following morning each pig was given 1 c.c. of an 18-hour growth of a pure culture of the organism isolated from the membrane of the conjunctiva. The protected pig was not ill. The unprotected pig died within 36 hours, and showed a local hemorrhagic exudate at the site of inoculation, general congestion of the viscera, and hemorrhage in the adrenals. An organism was isolated from the site of inoculation of the unprotected pig which was in every way similar to the diphtheria bacillus that had been subcutaneously injected. The above procedure was carried out three times, each time with the same results. The degree of virulence was very high.

A pig inoculated intraperitoneally with the water of condensation and surface contents of a 24-hour culture died within 6 hours from soluble toxins present. Some of the material from the same tube as that injected into the guinea pig was washed in salt solution and centrifugalized, and the supernatant fluid decanted. The precipitate was again washed and reprecipitated. Dilutions of these washed organisms when injected into an unprotected guinea pig killed the pig after 48 hours. The bacteriological diagnosis was a diphtheria bacillus of high virulence.

SUMMARY

Two cases of primary diphtheria of the conjunctiva are reported in a girl of 9 and a boy of 5 years. In Case 1, both morphologically and biochemically, the micro-organism was not typical; the guinea-pig test however left no doubt in the matter. The virulence of the micro-organism in Case 1 was mild, while in Case 2, the degree of virulence was high. In both cases examination failed to reveal diphtheria of any other part.

I wish to record my thanks to Dr. F. Smith and Dr. L. J. Rhea for their reports.

CYCLOPROPANE ANÆSTHESIA.—II. Killian discusses the chemistry, physics, and pharmacology of cyclopropane and reviews the accounts which have been published of this anæsthetic from Canadian and other sources. With the aid of a supply of the gas sent from America he has carried out animal investigations, self-administration, and a small number of surgical anæsthesias. His findings in the main support those of other observers—namely, that cyclopropane is a powerful

anæsthetic which must be used with due care, but that it is safe owing to the high degree of oxygenation permissible; it is without damaging effects upon the circulatory or respiratory systems. Clinically he has found the percentage of cyclopropane required to vary from 7 to 25, averaging 15 per cent cyclopropane to 85 per cent oxygen. He considers that the gas is a valuable anæsthetic, and hopes that further supplies will be soon available from German sources.—*Zentralbl. f. Chir.*, July 11, 1936, p. 1634. Abs. in *Brit. M. J.*

Clinical and Laboratory Notes

ENDOTRACHEAL ANÆSTHESIA SUPPLEMENTING AVERTIN IN OPERATIONS FOR CLEFT PALATE

By M. DIGBY LEIGH, M.D. AND
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Children's Memorial Hospital,

Montreal

In operations for cleft palate the anæsthetic must be adequate, it must be safe, and its induction should not frighten the patient.

In an attempt to find a satisfactory form of anæsthesia, a series of cases has been operated upon, using avertin by rectum, and combining it with nitrous oxide administered through a large endotracheal rubber tube by the technique of Magill. This method is adequate for the purposes of the surgeon, because the operation field is not encumbered by the anæsthetist or the apparatus. From the anæsthetist's point of view it is efficient in that aspiration or swallowing of foreign materials is prevented, and, in addition, intimate control of the supply of oxygen and nitrous oxide to the lungs is provided. In emergency, artificial respiration is easily carried out by intermittent manual compression of the bag. In the second place, the method is a safe one. When all the various sources of danger in cleft-palate surgery are considered, it can be said that the anæsthetic itself creates the greatest hazard to life. Meticulous preparation before operation can counteract the perils of sepsis, anæmia, and dehydration. Efficient treatment after operation for shock and hæmorrhage can be used, but the toxic effects of the drugs employed to produce anæsthesia always remain to be faced. There have been no deaths in the 32 cases covered in this report. The method has also been used in a large number of other operations upon the head and neck without misadventure. Thirdly, from the patient's point of view, this method of anæsthesia avoids the disagreeable features of ordinary induction

by inhalation. The avertin minimizes fear. A routine enema is always given before operation, and the child is not frightened when the rectal tube is again introduced some hours later for the instillation of the drug. Peacefully the patient slips into a sound sleep in its cot in the ward. After the operation it awakens in the same familiar surroundings. It has been saved the terrifying sounds and sights of the operating room and its environment. Avertin renders a special service in cleft lip and cleft palate, where a series of operations may be necessary, and where fear tends to be augmented with each successive trip to the operating room.

The procedure adopted is as follows. Prior to the operation the patient is examined in the ward by the anæsthetist, and the dose of avertin is calculated from the age and the weight. Infants are given 200 mg. of avertin per kilogram of body weight. The amount is reduced a little for each year, and at the age of twelve years, a dose of 100 mg. per kilogram of body weight is the standard. The weight of the child with respect to its age must also be taken into consideration. If the patient is found to be overweight for its age it is not advisable to give the full dose as calculated from age alone. Fat, or overdeveloped children should be given reduced doses. Conversely, children who are small for their age will require larger amounts of the avertin than would be indicated if age alone were taken as the guide. For example, a child twelve years of age, with the normal average weight of 36 kgm., would be given 100 mg. per kilogram: a small child of the same age, weighing only 28 kgm. should receive 150 mg. per kilogram.

The night before the operation the child is given its regular meal. About two hours later the lower bowel is carefully emptied by enema. The following morning, one-half an hour before operation, the determined dose of avertin is given in a 3 per cent solution. The largest soft rubber catheter that can be passed without dis-

comfort is introduced into the rectum. Using a funnel, the avertin is allowed to flow slowly into the bowel, and should the child struggle or cry the fluid can flow back into the funnel and not be lost. Ten minutes should be taken for the instillation. When the child is sound asleep a hypodermic injection of atropine sulphate is given to suppress secretions, and the patient is saved the pain of the needle puncture.

The patient is brought to the operating room. For palate operations a large thin-walled rubber catheter is passed through a nostril and made to enter the larynx, either by the "blind" method of Magill, or by the use of the laryngoscope and the Magill forceps. For lip operations it is passed through the mouth. If the first attempt to pass the tube through the larynx fails, open ether and carbon dioxide are administered to facilitate the intubation. As soon as the tube is in place it is wise to supply oxygen freely for a few seconds, and then to introduce nitrous oxide gradually. The pharynx is packed with a dry gauze sponge, to prevent blood from entering the stomach. The tube itself completely fills the glottis and protects the trachea. Partial re-breathing is carried out, using a bag about 12 inches from the face. Anaesthesia is maintained by supplying abundant oxygen with just enough nitrous oxide to keep the patient still. The use of avertin as a basal anaesthetic reduces the amount of nitrous oxide required, and, in consequence, increases the amount of oxygen that can be introduced into the lungs. Throughout the operation the patient remains in the supine position with the foot of the table slightly elevated. At the end of the operation the Magill tube is disconnected from the bag, and as it is withdrawn from the trachea, gentle suction is used to clear the air passages. To help restore body fluids and to combat post-operative acidosis, one-half to one pint of the fluid, as recommended by W. Bourne¹ in 1926, is instilled into the rectum. The patient is then returned to the ward. The arms are splinted to prevent interference

with the wound, and a nurse remains with the child until it is conscious. Voluntary movements usually begin within the first hour, and a small dose of morphia should be given if the patient becomes restless. Fluid nourishment, by feeder or pipette, is offered to the child as soon as there is any prospect of its being taken and retained. Solid foods are commenced as soon as possible.

SUMMARY

Since June, 1935, this method has been used in 32 cases, and the following information can be given:—

1. Age.—Youngest 7 months, oldest 14 years.

Ages	Number of patients
Under 1 year	4
Between 1 year and 2 years	3
Between 2 years and 3 years	6
Between 3 years and 4 years	7
Over 4 years	12
Total	32

2. Weight range—7 kg. to 56 kg.

3. Magill catheter passed through the nostril in 9 cases, through the mouth in 23 cases.

4. In three cases the avertin was partially expelled. Two of these patients were under 2 years of age. Expulsion can be stopped by squeezing the buttocks tightly together at the first sign of leakage.

5. Duration of operations, shortest 15 minutes, longest 90 minutes. Average time per operation 50 minutes.

6. Mortality: none.

7. Complications: one patient developed laryngitis and recovered in a week.

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EVIPAN SODIUM IN OBSTETRICS.—Dr. Van Boven strongly recommends evipan sodium anaesthesia for the short operations of obstetrics after an experience of about 150 cases comprising forceps delivery, internal version, suture of the perineum, Caesarean section, etc. His dosage has never exceeded 10 c.cm., and for full anaesthesia is as a rule twice the amount needed to

produce relaxation of the jaw. The advantages claimed are the peaceful and pleasant introduction, ease and rapidity of administration, single-handed if necessary, wide margin of safety, rapid recovery, and absence of ill effects on mother or child. He has had no difficulties or accidents, and considers the only contraindications to be advanced pulmonary or hepatic disease—*Bruzelles-Médical*, July 12, 1936, p. 1391. Abs. in *Brit. M. J.*

Editorial

ACETYLCHOLINE IN THE TREATMENT OF TOBACCO AMBLYOPIA

TOXIC amblyopia may be due to a considerable variety of agents, such as tobacco, alcohol, quinine, filix mas, carbon disulphide, nitro- and di-nitro-benzol, stramonium, cannabis indica, arsenic and lead. Of these causes the two first mentioned are much the most commonly met with.

The first references to tobacco amblyopia were made in Germany about the end of the eighteenth century; then in Scotland, in 1832, by Mackenzie in his "Diseases of the Eye". Since then much attention has been devoted to the subject but even yet it is not perfectly understood. We, however, realize that the ganglion cells of the retina and certain fibres of the optic nerve which pass from them are extremely sensitive to the action of various toxic substances. Some of these affect the peripheral cells and fibres and thus cause peripheral loss of vision, but the majority affect the central cells and fibres and cause central scotoma. Many years ago Unthoff noticed the curious fact that while the toxins which cause central defects of vision are competent to produce peripheral neuritis also tobacco was an exception to the rule. The toxin in this case, therefore, exhibits a definite selectivity analogous to that of the diphtheria toxin for the palatal motor nerves and for the third nerve, and to that of lead for the musculo-spiral nerve. The end-organ of the auditory nerve in the cochlea is also susceptible, apparently, for Carroll and Ireland¹ have recorded that deafness frequently accompanies the amblyopia associated with the excessive use of alcohol and tobacco.

Writing in 1928, H. M. Traquair² states that among 108,142 ophthalmological patients in Edinburgh he found 1,088 cases of tobacco amblyopia (1 per cent). F. D. Carroll,³ in 1935, met with it in from 0.3 to

0.5 per cent of patients admitted to the clinic of the Massachusetts Eye and Ear Infirmary. These figures seem to support the statement recently made, that, despite the enormously increased consumption of tobacco in the past few years, tobacco amblyopia is not so often met with as formerly. This is probably due to the fact that tobacco is nowadays consumed very largely in the form of cigarettes. Tobacco amblyopia is much more common, as a matter of fact, among inveterate pipe and cigar smokers than in the cigarette addict. It has been found also in chewers and snuffers. In as much as the use of snuff appears to be gaining in popularity we should be on the look out for cases among the devotees. Tobacco amblyopia is much less frequent in women than in men, probably because the former indulge in the cigarette rather than the pipe or cigar. Carroll (*loc. cit.*) gives the figures as 2 females in a total of 55 patients (3.63 per cent), and Usher⁴ found 2.5 of cases in females in a total of 1,100.

The amount of tobacco consumed in the Edinburgh cases (Traquair⁵) varied from $\frac{1}{2}$ to 9 ounces weekly per patient, the average being about $3\frac{1}{2}$ ounces. The smallest number of cigarettes found to produce the condition was 70 per week. Carroll and Ireland (*loc. cit.*), in 36 cases, found that the average amount of tobacco consumed was 8.9 ounces.

Some discussion has taken place as to whether so-called tobacco amblyopia is due to tobacco or to alcohol, for many excessive smokers also indulge freely in alcohol. Carroll (*loc. cit.*³) states that the average amount of pure alcohol consumed by his patients was 28.6 ounces per head weekly. He concludes that either tobacco or alcohol singly is competent to produce amblyopia. Traquair (*loc. cit.*⁵) thinks that, so far as Scotland is concerned, there is no relation-

1. CARROLL, F. D. and IRELAND, P. E.: Association of toxic deafness with toxic amblyopia, *Arch. of Otolaryngol.*, 1935, 21: 459.

2. TRAQUAIR, H. M.: Tobacco amblyopia, *The Lancet*, 1928, 2: 1173.

3. CARROLL, F. D.: Analysis of fifty-five cases of tobacco-alcohol amblyopia, *Arch. of Ophthalmol.*, 1935, 14: 421.

4. USHER, C. H.: An analysis of the consumption of tobacco and alcohol in cases of tobacco amblyopia, *Ann. Eugenics*, 1927, 2: 245.

5. TRAQUAIR, H. M.: Tobacco amblyopia, *Trans. Med. Chir. Soc. Edin.*, 1934, 35: 153.

ship between tobacco and alcoholic amblyopia, and gives what appear to be satisfactory reasons from clinical experiences for his opinion. No doubt, the two agents can act synergically on occasion. In any case, something more than a toxin seems to be necessary, probably a personal idiosyncrasy or some depressing external agency. Cases are known where those who have indulged excessively in tobacco for years with impunity have not developed amblyopia until attacked by some other illness or a digestive disturbance.

As regards treatment, naturally the first thing to do is to interdict the use of alcohol and tobacco. Drugs can be employed rationally only if we understand the pathogenesis of amblyopia, and, unfortunately, we are still somewhat ignorant of this point. So far as the early stage is concerned, inasmuch as patients do not seek advice until they themselves detect something wrong with their vision any pathological alterations in the eye are likely to be well advanced, and the initial manifestations will have been missed. We can draw conclusions only from ophthalmoscopic appearances, and then by inference. Even at this time the changes observed are slight, consisting in a congestive haze of the edges of the optic disc followed by undue pallor of the temporal side of the disc. In the one human case where the eye was examined microscopically the ganglion cells of the retina showed vacuolation and disintegration of the Nissl bodies with degeneration of the nerve fibres behind the lamina cribrosa. This degeneration was limited to the papillo-macular bundle. Possibly we are justified in concluding that the ophthalmoscopic picture is due to the occurrence of local atrophy of the retina plus an œdema which causes an anæmia from pressure. If so, we can justify the use of agents which can set up vaso-dilatation, as certain have advocated, such things as sodium nitrite and the presently popular acetylcholine.

Sir Stewart Duke-Elder,⁶ who has investigated the subject experimentally, states that choline and acetylcholine act as powerful stimulants on the parasympathetic nerve

apparatus, producing contraction of the sphincter and ciliary muscle. They also dilate the small vessels, unless atropine has been exhibited previously, in which case a constrictor action is set up. In small doses choline lowers intra-ocular pressure; in large doses it causes a sudden and considerable rise in the pressure in the eye owing to the contraction of the extra-ocular muscles which is induced. Theoretically, on this basis, small doses of acetylcholine might be expected to do good in amblyopia by relieving pressure on the retinal cells and improving the circulation in the retinal blood vessels. The experiences of two or three observers may be cited in this connection. Bailliart and Rollin⁷ report a case in which the left eye was affected; twenty injections of acetyl chloride were given with some relief of symptoms but no change in the field of vision. Marchesini⁸ found, in six patients with retinal angiospasm, that the administration of acetylcholine produced a fall of blood pressure much greater than normal, on the average amounting to 2.16/10 for right eyes and 1.5/10 for left eyes. Orr,⁹ of Wolverhampton, has very recently reported on four cases of tobacco amblyopia which he treated with acetylcholine with gratifying success. All his patients were advised to stop smoking, but abstinence was not complete. He thinks that if his results can be confirmed by other ophthalmologists we shall have in acetylcholine the best agent for the treatment of tobacco amblyopia. On the other hand there are competent men who deny that vaso-dilator drugs are of any value in this condition. Only time will settle the matter. There is difficulty here in evaluating the effect of any drug, inasmuch as tobacco amblyopia, provided that abstinence is adhered to, is variable in its course and tends of itself to get well. If acetylcholine can speed up the process of recovery the case for it will have been made out.

A.G.N.

6. DUKE-ELDER, SIR S.: *Recent Advances in Ophthalmology*, P. Blakiston's Son & Co., Inc., Phila., 1934, p. 144.

7. BAILLIART, P. and ROLLIN, A.: *Spasm of retinal arteries*, *Bull. Soc. d'ophl. de Paris*, 1935, Oct., 612.

8. MARCHESINI, E.: *Retinal arterial pressure in relation to the general circulation and to certain ocular diseases*, *Ann. di Ottol. e Clin. ocul.*, 1935, 63: 532 and 621.

9. ORR, H. C.: *Acetylcholine in tobacco amblyopia*, *Brit. M. J.*, 1935, 2: 69.

POISONING BY MUSSELS

THE report that poisoning from eating mussels has occurred in Nova Scotia is of more than ordinary interest. Five cases have been met with, we are informed, of which two ended fatally. So far as we can learn, this is the first time within recent years, at least, that mussel poisoning has been met with in Canada. The occurrence is being investigated.

Between the years 1798 and 1928 there have been twenty-one outbreaks of this trouble in Europe and North America—10 in Great Britain, 7 on the Pacific coast of North America, 2 in Prussia, 1 in France, and 1 in Norway—embracing a total of 244 cases with 38 deaths.¹ In the California outbreak 102 persons were affected of whom 6 died. The species of mussel incriminated is the *Mytilus edulis* in Europe and the *Mytilus californianus* in California. Since then other cases have occurred in California, 55 in 1929, one in 1930, two in 1931, and 42 in 1932.²

Meyer, Sommer and Schoenholz¹ refer to a book entitled "Vancouver—A Voyage of Discovery to the North Pacific Ocean", London, 1798, in which an illness is referred to affecting several members of an English expedition to the north-west coast of America at a place now known as Vancouver. One death occurred. These authors say that the onset and course of the intoxication identify it with mussel poisoning as they saw it in 1927.

Poisoning from eating shell-fish may be divided into three categories: (1) cases due to allergic idiosyncrasy, which are attended by the relatively mild disturbances, urticaria and gastro-intestinal upset; (2) infective cases, due to contamination with various members of the Eberthella and Salmonella genera of bacilli—traceable to contamination with sewage; and (3) cases in which the nervous system is predominantly affected, manifested by paræsthesiæ, paralyses, and sometimes death from respiratory failure. The Nova Scotia cases fall into the last group.

Most textbooks mention mytilotoxin, a quaternary base, isolated by Brieger in 1888,³ as the probable cause of the trouble, but subsequent observers have failed to identify the toxic substance found in the paralytic cases with Brieger's substance. The poison isolated from the cases in California is similar, chemically and pharmacologically, to the "fugu" poison of Japan, obtained from the liver and gonads of certain species of *Tetrodon*, which is used by the Japanese as a convenient and rapid method of committing suicide.⁴ In nearly all cases the liver of the toxic shell-fish is enlarged, friable, and of dark colour, a fact that suggests the possibility of some disease condition, bacterial or metabolic. No bacteria, however, have been incriminated in the "paralytic" cases, though, it must be said, the possibility of a virus being the cause has not been excluded. Inasmuch as the toxic mussels in the California outbreaks were always full of spawn Meyer, Sommer, and Schoenholz (*loc. cit*) thought that the toxin was a "sex poison". Suggestive analogies are found in the fact that the roe of some fish of the sturgeon family is poisonous during the spawning period. Prinzmetal, Sommer and Leake,⁵ on the basis of experimental evidence, think it unlikely that the poison is histamine. Mussel poison is many times more toxic for mice than histamine on intraperitoneal injection, and differs from histamine also in the fact that it has no noticeable action on smooth muscle. In general it resembles curare and is probably a quaternary (or possibly tertiary) amine. The toxic material from the poisonous mussel is slowly absorbed from the gastro-intestinal tract and is rapidly excreted through the kidneys. Its main action seems to be to depress respiration. The cardio-inhibitory and vasomotor centres are also depressed, as is the conductive system of the myocardium.

1. MEYER, K. F., SOMMER, H. and SCHOENHOLZ, P.: Mussel poisoning, *J. Prevent. Med.*, 1928, 2: 365.

2. MÜLLER, H.: Mussels and clams: a seasonal quarantine: bicarbonate of soda a factor in the prevention of mussel poisoning, *California and West. Med.*, 1932, 37: 263 and 327.

3. BRIEGER, L.: Zur Kenntnis des Tetanin und des Mytilotoxin, *Arch. f. path. Anat. u. Physiol. u. f. klin. Med.*, 1888, 102: 549.

4. PHISALIX, M.: Animaux Venimeux et Venins &c., Masson, Paris, 1922.

5. PRINZMETAL, M., SOMMER, H. and LEAKE, C. D.: The pharmacological action of mussel poison, *J. of Pharmacol. and Exper. Therap.*, 1932, 46: 63.

6. MÜLLER, H., *loc. cit*.

Soon after the ingestion of poisonous mussels, and the more quickly if the stomach is previously empty or if no other food is taken, the patient notices numbness of the mucous membrane of the mouth and numbness and pricking of the fingers and toes. Then, incoordination of the movements of the limbs, ataxic gait, and incoordination of speech are noted. The early manifestations have a striking resemblance to acute alcoholism. The mind is clear, but the patient may feel exhilarated and may not realize the seriousness of his condition. Nausea, vomiting and diarrhoea are occasional phenomena. A gripping sensation in the throat and respiratory distress have been observed. In fatal cases pareses of the musculature of the neck and limbs, with dyspnoea, and, finally, respiratory paralysis may occur. Death has occurred in as short a time as three hours. The average temperature is slightly subnormal; the pulse is increased in rate, from 80 to 100.

The treatment consists in washing out the stomach with a solution of bicarbonate of soda and the exhibition of saline cathartics, such as Epsom salts, and powerful diuretics. If the depression of the respiratory centre is marked carbogen and coramine are indi-

cated; artificial respiration may be called for. Digitalis and alcohol should not be used.

The greatest number of cases of mussel poisoning occur in summer, in some years as early as June and as late as September. Consequently, the California Board of Health has instituted a quarantine on mussels during the summer months every year since 1927, and a few years later this was extended to cover clams, which also have been found poisonous at times. The usual methods employed in cooking mussels and clams do not lessen the danger of poisoning. The water in which the shell-fish are boiled or which remains in the shells should be thrown away, as it contains a large proportion of the poison. The addition of soda bicarbonate, a tablespoonful ($\frac{1}{4}$ oz.) to each quart of water in which the mussels are cooked, is advisable since boiling continued for 20 to 30 minutes destroys 85 per cent of the poison, though it does not altogether obviate the danger. In the case of both mussels and clams the poisonous substance seems to be confined almost entirely to the intestines, so that these organs should be removed before the shell-fish are cooked. This is an easier procedure in the case of clams inasmuch as in them the intestines are relatively large and easily detected.

Editorial Comments

The British National Human Heredity Committee

In England, a National Human Heredity Committee has been formed, composed of R. Ruggles Gates, Sir Humphry Rolleston, Grafton Elliot-Smith, R. A. Fisher, Sir Arthur Keith, and Sir F. Gowland Hopkins. They have sent a letter to the Editor of the *London Times* which reads as follows (quoted from *Science*, June 5, 1936).

"Problems of national health have reached a point where the hereditary element can no longer be neglected. The leaders of the medical profession are no longer satisfied with the alleviation of disease but are acutely conscious of the need for fuller knowledge of heredity in connection with its prevention. This applies not only to the transmission of defects. It is recognized that methods of cure must vary with the type of constitution of the patient, and in this connection information concerning heredity is of great importance. In education, in training, and

in choice of career the ascertainment of innate endowment not only prevents waste and failure but would contribute largely to the attainment of success.

"The instructed public already recognize the importance of heredity for the future of the race, and the Broek report in 1933-34 emphasized the need for greater knowledge in regard to the inheritance of mental and physical defects. But there is as yet no centre to which the public can turn for full information.

"The Imperial Bureaus of Plant Genetics (in Cambridge and Aberystwyth) and of Animal Genetics (in Edinburgh) have achieved much by setting up simple machinery for collecting information based on the results of research and making these available for the practical breeder. The Bureau of Human Heredity which has recently been set up at 115, Gower Street, W.C.1, follows these models, and small contributions have already been made for its upkeep.

"In these days of international mistrust and animosity it is refreshing to find a field in which

representatives of nearly every civilized nation are engaged in cooperative work. The scheme for an international clearing-house of facts concerning human heredity has been evolved by a small international committee, which has delegated to its British members the task of setting up a bureau in London for the collection and distribution of all authentic information on human genetics. The British Council is asking for £10,000 to carry on this work for five years.

"It is strange to think that students of fruit-flies or mice have at their command the latest information, while those similarly concerned with man can look nowhere for a complete survey of the knowledge they require. The urgency of this need leads us to commend the Bureau of Human Heredity to public-spirited donors. They will find no institution the endowment of which will give a more liberal return for all time."

For some years, we have been urging upon the medical profession, especially those connected with the teaching of medicine, that a course in Medical Genetics be included in the medical curriculum, which will enable the physician of tomorrow to be more conversant with the subject of heredity in man than he is at present. As Lord Horder has said, there would be time for such a course if other subjects, less important than human heredity, were left out of the curriculum or curtailed in time. It is to be hoped that Canadian medical schools will sponsor such a course in medical genetics (this subject is already being taught in several of the leading American schools), and that Canadians in general will sponsor such an institute for the study of human inheritance as has been founded in many of the European countries and is now being founded in England. The distinguished names on the committee in Great Britain may be taken as an index of the importance of the plan they urge. Why should not the Canadian medical profession get behind the same movement in Canada?

MADGE THURLOW MACKLIN

Medical Science Exhibits

We have become so accustomed to the medical exhibits at annual conventions that we take them for granted. And yet, it is doubtful whether medical men in general realize what work lies behind them or how greatly the technique of their presentation has improved. Those

who attended the Conjoined Meeting at Atlantic City last year had full opportunity of seeing these things for themselves, and we understand that the exhibits at the Kansas City meeting of the American Medical Association this year fully sustained the standard set.

We are reminded now of the medical exhibits at the Century of Progress Exhibitions in Chicago, in 1933 and 1934, by a booklet in which they are preserved in pictorial form. One cannot look through it without a freshened sense of the importance of such exhibits. These at the Chicago Exhibitions were unusual in being the first attempt of the kind in connection with an international exhibition in America, but the principles underlying their value were the same.

In getting out this most attractive booklet the aim has been to prolong the influence of these exhibits and also to help towards the foundation of permanent museums of health. The value of such can hardly be overestimated in instructing public opinion in matters of general health. They serve also to show the public just what immense and varied labour lies behind the training of the qualified practitioner, nurse, dentist and pharmacist, serving to sharpen the contrast between them and the untrained quack. We can only add that the pictures of which this book is composed entirely and most attractively perform their function in describing the variety of the exhibits, incidentally causing one to marvel at the labour they must have entailed. H.E.M.

Income Tax Allowance for Automobiles

We are in receipt of a letter from Mr. C. F. Elliott, Commissioner of Income Tax, Ottawa, addressed to the General Secretary, which reads as follows.

"With regard to Clause 2 (i) of the Memorandum regarding Returns of Members of Medical Profession, issued under date of 28th February, 1933, wherein it is stated that as an alternative to (h) and (i) there may be allowed a charge of 10 cents per mile for automobiles used in the performance of professional duties, it may be said that as a result of experience since that memorandum was issued it is felt that the 10 cent per mile is a too liberal allowance, and while it is not proposed to reduce this allowance retroactively, yet the Department has come to the conclusion that for 1936 and subsequently this allowance shall be reduced to 8 cents per mile."

* Medical Science Exhibits. Eben J. Carey, Sc.D., M.D. 204 pages, illustrated. Price \$2.00. Copies may be obtained from Patrick J. Byrne, 624 S. Michigan Ave., Chicago, 1936.

Generally speaking we might say that the diseased employ a language which corresponds to thinking, to concepts that are at a lower level, or at least of a different order of abstraction. Just as one cannot measure apples by a foot-rule nor describe books in

terms of Turkish rugs so the language of disease is not susceptible of a literal, word-for-word translation into the language of the well. A translation of what the sick person is trying to convey in what he says is quite the same sort of process as the translation of a primitive language.—White, *The Meaning of Disease*, p. 150.

Special Article

THE RELATION BETWEEN PSYCHOLOGY AND MEDICINE*

By S. R. LAYCOCK,

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Saskatoon

Because there are so many misconceptions of the nature of psychology, and because psychology has undergone in the last few decades a change amounting to a revolution, I feel that I must begin my address by a brief statement of what psychology really is. First of all, it is not, as it was in the university days of some of the members of this audience, a branch of philosophy. As you know, all branches of knowledge were once a branch of philosophy. In the days of the Greeks, physics, chemistry, astronomy and geology were all parts of philosophy. Leucippus and Democritus, for example, expounded the atomic theory of matter as philosophers. Anaximenes, a philosopher, thought the visible dome of the sky was half a complete sphere with the earth at the centre. Empedocles, a philosopher—not a chemist—thought earth, air, fire, and water were the basic elements out of which all other substances came. One by one the sciences of physics, chemistry, astronomy, biology, left the parental roof of philosophy and set up in business for themselves. Psychology was one of the younger members of the family, one of the last to leave. In other words, in the last few decades psychology has become a science.

The difference between science and philosophy is this. In philosophy the results are obtained by speculation and introspection, in science, by controlled experiment; in philosophy deductive reasoning is very common, while in science there is the inductive approach. The scientific method involves (1) accurate observation of a large number of facts, (2) classification of those facts, (3) the formulation of a hypothesis to explain the facts, (4) verification of the hypothesis, (5) the formulation of general laws. Psychology is rigorously trying to follow this method. A science is not characterized by the nature of its subject matter but by the method of its attack.

Psychology has had a harder job in making progress than the older sciences because it has had to combat theories about human nature and conduct and about the human mind which are very thoroughly established and which are the results of theological and philosophical

speculation. For example, in the field of the law jurists had to have theories about human nature before scientific psychology could supply them, and, as a result the law is established on deductive and theological conceptions, and the time has now come when all legal conceptions have to be worked over in terms of modern psychology—such doctrines as responsibility, free will, motivation, etc.

Next I want to say that psychology is not a science of the soul or of the mind, since no one knows the nature of these, nor is it the science of consciousness, as some of you learned in your university days, since there is a whole psychology of the unconscious. Rather modern psychology regards itself as the science of *behaviour*, and by behaviour it means muscular, glandular and cortical reactions. It accepts as its fundamental hypothesis the foundation of *all* science, namely, that of cause and effect. The natural scientist assumes in the material universe that cause and effect operate, and all advance has been made on that basis. Similarly, scientific psychology, leaving aside mysterious problems of free-will, intuitions and "hunches", objectively studies behaviour on the assumption that *all* behaviour consists of reactions to stimuli. In primitive times behaviour was considered as the result of one of three agencies—(1) human agencies by magic, (2) supernatural agencies, (3) natural causes. The man on the street still thinks of human behaviour in these three categories, but modern scientific psychologists go only on the last—natural causes.

Our approach to behaviour and conduct disorders is now the same as yours, i.e., the diagnostic point of view. When you, as physicians, go to see a patient and you find he has a temperature of 102° you do not just say "naughty, naughty", you proceed to diagnose the underlying causes. Similarly, the clinical psychologist dealing with a behaviour problem like stealing regards it as merely a *symptom* of social maladjustment and proceeds to look for underlying causes. Courts and parents and even teachers often treat *symptoms* instead of underlying conditions. For example, you as physicians may have ten patients all with a temperature of 102°. How ridiculous it would be if you stopped at the taking of the temperature and gave all the same medicine. But that is what has been done with behaviour. Stealing isn't just stealing—it may be due to as wide a variety of causes as a temperature of 102°. Child Guidance Clinic annals reveal that stealing may have its roots in the child being undernourished and not having enough food, in sex-behaviour and conflicts, in subtle motives of revenge against parents, in attention-getting mechanisms, and in compensations for feelings

*An address delivered before the Prince Albert and District Medical Association on December 10th, 1935.

of inferiority occasioned in dull children by our present uniform curriculum, organization and teaching methods in schools. If I had time I would show you how truancy is just a symptom of school maladjustment, due to a large variety of causes, and how laziness, inattention, and lack of concentration are just blanket terms for lack of interest and where underlying causes must be sought.

I wish, too, that I had time to show you in some detail the things we use in diagnosis. You, as physicians, use a wide range of examinations in diagnosis—increasingly objective—blood counts, urinalysis, basal metabolism, x-rays, etc. I would have liked to have told you how I use the facts of the school history, the results of the medical examination, intelligence tests, achievement tests, reports and ratings by teachers, reports and ratings by parents, developmental history, family history, and an interview with the child.

May I point out we are moving in the same direction as medicine, towards increasingly objective and scientific methods in diagnosis.

And now let me turn to the other part of my address, the relation between psychology and medicine. I am not going to enter into the ancient controversy—the mind-body controversy, though it is obviously very important what you think about it. Perhaps it is sufficient to say that the Christian Scientist who denies the existence of matter and affirms the universality of mind, and who replaces all medical treatment of disease with a system of faith cure or mental treatment, is not much worse than a thoroughly materialistic materia medica which limits the healing art to the drug or surgical treatment of the malfunctioning organ, and which undervalues or completely neglects the treatment of the patient as a whole, as a functional unit. Fortunately, this crass materialistic treatment, followed, I hope, by a limited number of the disciples of medicine, is now declining.

Modern psychology conceives of the human organism as a highly complex ensemble of mental and physical traits and functions that are inextricably intertwined and interdependent. It believes that these factors exert a reciprocal influence upon one another and are mutually affected by numerous environmental and hereditary influences which conduce towards mental soundness and unsoundness. The human organism is a psychophysical unity. The physical and mental are merely two aspects of the same unitary organism, just as the obverse and reverse are merely two sides of the same shield, the one as indispensable as the other. If, then, the assumption is correct that the body and mind are mutually interdependent and interacting aspects of a single organism it logically follows that any program for the attainment of health that neglects either the mental or physical factors is incomplete and unsatisfactory.

I do not need to remind you as physicians of the influence of the so-called physical aspect on the so-called mental aspect of the organism. Bodily diseases, injuries and defects sometimes produce sudden and profound mental disturbances, and therefore seriously affect behaviour. As examples of this I may cite the following: delirium as an effect of fever; a blow on the head or the bursting of a cerebral blood vessel may produce sudden stupor or unconsciousness; excessive fatigue may produce inattention, muscular incoordination, memory lapses, temper tantrums; jaundice does not conduce to generosity or philanthropy; heart sensations may induce anxiety and apprehension; disturbances in the endocrines always have mental concomitants; for example, excessive thyroid secretion in exophthalmic goitre tends to induce nervous and mental instability, sleeplessness, emotional instability.

Another line of evidence in regard to the effects of the physical upon the mental concerns the influence of foods and drugs upon mentation. Certain foods, even such as milk, eggs, or mushrooms, may in certain cases produce epileptic convulsions. Certain foods have been found to inhibit sex activity in rats. The effects of alcohol, inducing loss of motor control, thick speech, mental confusion, forgetfulness, excitement, depression, etc., are well known. I do not need to multiply instances. You know more than I do in this field.

But what about the influence of the mental upon the physical? Here I think, too, the evidence is indisputable, not only for the widespread somatic reverberations of emotional experiences but also so far as it concerns the mere emotionless thinking or attentive states upon the circulation of the blood or upon motor innervation. That mere thought or ideas can affect the circulation of the blood through the excitation of the nervous system can be shown by the well known balance board experiment. In this experiment the subject, while lying quietly upon a perfectly balanced platform, is asked to read an unemotional passage of prose or solve a mathematical problem. After a brief interval the experimenter will observe that the end of the board on which the head rests gradually begins to descend. Obviously, thought has affected the circulation; it has caused the blood to flow to the head, in consequence of which the head grows heavier and the board begins to tilt.

Similarly, if attention is concentrated upon an active muscle the flow of blood can be increased to that muscle. The effect of attention upon the circulation can be most convincingly shown in states of hypnosis in which the subject becomes highly susceptible to suggestion. In some cases the mere suggestion by the hypnotist that the subject has a scar or burn on the arm may produce a localized area of hyperæmia on the skin. This is the obvious explanation of many hysterical symptoms. However, the most

striking illustrations of the influence of the mental upon the physical are not derived from a consideration of processes of calm logical thinking or of perceiving and attending. It is when mental processes are closely connected with instinctive functions and glandular activities that the effect of mental states upon physical conditions become more clearly apparent. In a general way, any mental activities that stimulate the endocrine glands will exert a subtle influence that may pervade the whole organism and sometimes may produce the most profound organic disturbances. The extreme sensitivity of some of the glandular functions to mere ideas or perceptions is well recognized. In some persons, for example, the sex centres in the brain and the cord are so responsive that mere images and thoughts can serve as adequate crogenous stimuli. Also, the mere thought or perception of appetizing or unappetizing foods or of savoury or unsavoury odours is sufficient to stimulate the salivary or gastric nervous centres in many persons.

Wallin quotes a well known experiment upon a dog in which the gastric secretion was diverted into a container instead of the stomach. An undisturbed, pleasurable five-minute feeding resulted in the secretion of 66.7 c.c. of gastric juice in from fifteen to thirty minutes. On a later occasion, when the dog became excited by being shown a cat just before the feeding, no secretion occurred during the five-minute feeding period, and the secretion amounted to only 9 c.c. in the following twenty minutes. Emotional excitement inhibits the flow of gastric juice.

Emotional experiences are the chief cause of nervous dyspepsia or acute indigestion rather than the food ingested. An instance, cited by Wallin, is that of a woman brought to the hospital because of an attack of acute indigestion. It was found the following morning that the evening meal had remained in the stomach all night. Further investigation disclosed that she had been upset in the evening by a quarrel with her husband who had come home drunk.

The profound organic commotion that can be produced by intense emotional experiences can be illustrated by fear. Not only is fear evidenced by trembling, shrinking, raising the eyebrows, irregular breathing, and by movements of escape or combat, but also by inner conditions such as dryness of the mouth due to inhibiting action upon the salivary glands, inhibition of the flow of gastric juice, and acceleration of heart action with consequent rise in blood pressure.

Cannon has found in experiments that the strong emotions—fear, rage, excitement, anxiety, worry—cause the adrenal glands to discharge excessive amounts of adrenalin. This seems to shut off the activities of digestion and stimulates the heart and lungs to strong action. Further, it makes the liver secrete its store of blood sugar

required by the muscles. In other words, the strong emotions constitute a calling out of the troops. In primitive days when attacked by an enemy the animal had to mobilize all its reserves for either fight or flight. And it could afford to have its digestion switched off temporarily, since, obviously, if one was to be eaten by a beast of prey it wouldn't matter whether one's dinner digested or not. In contradistinction to the strong emotions which deplete the body reserves, the mild emotions of mirth, joy, goodfellowship, stimulate the digestive activities and to some extent allow the troops to loaf in barracks. In other words, the strong emotions use up reserves and the mild emotions build them up. This has tremendous implications for physicians in two ways. (1) The effects of emotional upheavals of fear, anger, rage, grief, worry, and anxiety may give rise to or at least aggravate stomach trouble, indigestion, metabolic disturbances, diabetes or glycosuria (mentally disordered persons subject to fears often suffer from diabetes), overaction of the thyroid and adrenal glands, loss of vitality, jaundice, heart disorders, degeneration of the liver, insomnia and dysentery (a defeated army suffering from dysentery is more likely to be suffering from mental collapse than from intestinal infection). Symptoms which simulate those produced by organic disturbances are everywhere to be found.

The exhausting and disturbing effects of emotional upsets upon the nervous, glandular, digestive and circulatory systems may lead to nervous exhaustion or hyperexcitability as well as to nervous maladies. Nervousness in general is due more frequently to emotional stresses and adjustment difficulties than to physical disease or injury, although physical derangements aggravate the condition. Nervousness is not really a disease of the nerves. It is a disorder of function rather than a defect of structure. It is more of an emotional than a physical disorder. Ninety per cent of the cases of shell shock in the World War were due not to any physical injury received in battle, but to disturbed emotions and to emotional collapse from fear, anxiety, dread, and the desire to escape from the battle front. J. W. Barton has estimated that over fifty per cent of all patients consulting physicians or seeking hospital treatment have no real organic trouble. E. A. Strecker believes that fully fifty per cent of the problems of the acute stage of illness and seventy-five per cent of the difficulties of convalescence have their primary source in the patient's mind rather than in his body. Maurice Craig says that from fifty to seventy-five per cent of the patient's illness may be due to his attitude towards his disorder. It is notorious that the patient's attitude to his illness is often harder to treat than the sickness itself.

I like to think of the word disease in its root meaning, dis-ease. Now dis-ease may be either physical or mental. It will be obvious

from the above that no physician can hope to treat his patients adequately unless he is first of all willing to recognize that emotional upsets and conflicts, strains, shocks, worries and anxieties may be at least definite contributory causes to the disorder he treats. His diagnosis is incomplete without a psychological diagnosis, and his treatment is incomplete without psychological treatment.

Most physicians pick up quite a bit of practical psychology from practice, but it is also true that most physicians are quite innocent of the findings of modern psychology or of recent developments in psychopathology and psychotherapy. It is not enough to use this unconsciously. The medicine man of primitive tribes and the Christian Science practitioner use psychology unconsciously. Speaking as a layman, may I humbly suggest that training medical students in psychiatry, which usually means the psychotic condition of advanced mental disease, is not enough. What a medical student needs is a grounding in the psychology of the so-called normal people—the people who come to his office from day to day. Psychology as an applied science now exists and it can be applied to medical practice.

(2) A second implication of any discussion of the effects of emotional stress on physical condition lies in the fact that since fear, for example, calls out the body reserves and the body-destroying processes, and since the mild emotions of mirth, joy, and goodfellowship call out the body-building processes, then it is the physician's duty to get nature working with him and not against him. Confidence in the physician is therefore of great value. When patients come to you and talk to you they often go away feeling much better because they have talked to you, even when you have given them no medicine or treatment, because you have removed their fear and let nature have a chance. You visit your sick patients regularly not only because it is necessary to see how they are getting along but to remove their fear and anxiety and give nature a chance to work. Apart entirely from the legitimate uses of medicine, x-rays, etc., there may be definitely a beneficial effect because they remove fear and lurking unknown terrors. Doubtless, a host of patent medicines and quack remedies flourish because they have helped people through the removal of fear and letting nature have a decent chance. May I respectfully suggest that until the science of medicine is able to take up into itself psychotherapy, and to do it wisely, quacks of all sorts will continue to flourish.

All of this will have to be handled with skill and understanding. There is always the danger in connection with even such worthy causes as the cancer campaign that, in trying to educate people, you merely succeed in implanting fears, with all sorts of disastrous results.

Sometimes, too, physicians, instead of inspiring confidence in themselves, succeed merely

in making the patient believe he is terribly ill, with consequent fears. It is a bit of a dangerous game to play a corresponding role to some professional evangelists who work up guilt feelings in order that they may prescribe their own pet remedy. In fact, the treatment given a patient sometimes depends on the personality and personal maladjustments of the physician as well as on the condition of the patient. Already it is advocated that all teachers have a psychiatric examination before being licensed. Some day this will also apply to nurses and physicians.

I am far from suggesting that fear and anxiety are the only mental elements in producing disease. Mental conflicts of all sorts are fruitful sources of illness. Some are conflicts over sex; some are conflicts over the attitudes towards the self; and many illnesses are unconsciously wished for illnesses which offer a way out. An example of this, quoted by Wallin, is that of a badly pampered young man, of somewhat unstable type, who began his career as an accountant. Before many weeks he was brought home complaining of severe pains in the eyes and in the right arm, which seemed partly paralyzed. Feeling better after a few days' rest, he returned to work, only to find the attacks recurring. The significant thing about these symptoms is that they made his work at the office impossible. Actually, the young man found the tedious task at the desk, day in and day out, extremely boring, and the work deprived him of the freedom and comforts which home life had previously given. At the same time, he was naturally averse to quitting outright. That would offend his self-respect and bring the scorn of his friends as well. Perhaps one afternoon the fatigue of eye and hand did become severe, providing an excuse for release from labour for the day. The next day the same symptoms occurred in more severe form, and half frightened, and yet half gratified, he was taken home. Not only did he thus escape the unpleasant work but the criticism of himself and others as well. In fact, he reaps more sympathy and care than ever. To refer again to the neuroses of the war. All sorts of *physical* symptoms, paralysis of the arm, temporary blindness, vomiting, etc., provided an unconscious defense mechanism. I am not maligning soldiers, for I am a returned man myself.

Faith cures of all sorts, which since the days of the medicine man of primitive tribes and of heathen rites and the oracle at Delphi down to modern Christian healing, are not mysterious cures of a supernatural order; they are a species of psychological healing in which either (1) the conflict is resolved, or (2) the patient gets more satisfaction out of being well than out of being sick, or some similar psychological process. These forms of healing often embarrass medical men. They should not. The problem is not solved by saying it is just "mental". The medical profession must do the same thing, only scientifically, and, if scientifically, in the long run better.

We need psychotherapists—medical men who really know a lot of normal and abnormal psychology—not merely medical men trained in the end-product of mental disease. And since the individual functions as a psychophysical unity no physician can treat just *physical disease*, he must treat *persons*. Whether you realize it or not, you *must* use the psychological element in your work. My plea is that the medical profession use it scientifically and consciously instead of empirically and unconsciously. Many hospitals now use the services of a social worker as part of their therapeutic service. May I suggest that the time will come when every physician with a large practice will have a trained social worker to assist him.

May I suggest also another point of view. Just as it would be difficult for you to divide the population into two classes, the sick and the well, but rather into a whole series of less and more well, so a study of individuals on the mental side presents a continuous gradation all the way from so-called normal people to the violent patient in the mental hospital. The difference between the insane and us are only those of degree and of kind. Differences are quantitative, not qualitative. Everything we have in a mental hospital we have in milder degree in life. Grandiose delusions are but an extreme form of the "livelightiness" of some school children, and everyone of you knows of themselves more highly than the facts warrant. The grandiose delusions have their counterpart in life in the neurotics who are very suspicious and think that everyone is "down" on them. The "livelightiness" abundantly in school children and in a large percentage of adults, is merely a mild form of grandiose delusion. The child with temper tantrums and the adult who goes "clean off his head" with rage are milder forms of a manic phase found in mental hospitals. So psychoanalysts and mental hygienists think of self-pity, temper tantrums, sullenness, sulkingness, shyness, livelighiness, feelings of inferiority and superiority, resentment, pouting, as mild disorders, all more or less mental. So the problem of the prevention of mental disorders goes down into early childhood into the school and home, and it isn't only their mental health—it's their *health*. No child can be said to be *healthy* when it suffers from such emotional maladjustments as described above.

In conclusion, may I make a plea for the treatment of behaviour, personality or conduct disorders on an objective basis. To tell persons with neuroses that they are ridiculous or silly or blameworthy doesn't solve the problem. Rather these people need diagnosis, understanding and *treatment*. To tell a person with a pain that it is just imaginary and he is to forget doesn't solve the problem. It only sends him off to another doctor or, worse still, to the quacks.

One must, however, be equally warned against the opposite extreme, *i.e.*, admitting that the patient has a pain and pretending to know all about it, ascribing it to an organic source and operating, leaving the patient no better. If there is no organic basis for the pain there may be a psychological one, and telling the patient to forget it does not remove it in this case any more than when there is a physical basis. The people with neuroses are not to be made to feel inferior and culpable. They need and deserve treatment just as your other patients need and deserve treatment.

To assume that *all* forms of behaviour are amenable to the law of cause and effect is the approach of a scientist. Medical men must treat individuals, and the day must come when their understanding and therapy are as scientific in the so-called mental realm as in the so-called physical realm.

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SOME PERSONAL IMPRESSIONS OF THE MEETING OF THE BRITISH MEDICAL ASSOCIATION HELD IN OXFORD IN JULY, 1936

By ROBERT DAWSON RUDOLF,
Toronto

The 104th Meeting of the British Medical Association was held in the classical surroundings of Oxford this year and was as usual well attended and a great success. The first few days were taken up with the work of the Council, and most parts of the Empire were here represented, but Canada had no voice. It seems to be a pity that the numerous members of the Association who live in Canada should have no say in such an important conference, but such is at present the case. The delegates from the Canadian Medical Association (Drs. Birkett, A. H. Gordon, and the writer) were of course welcomed and duly presented to the President at the Annual Meeting, but they had no official position as representatives of the members of the Association in Canada, and therefore no *entrée* to the Council meetings where all the activities of the Association are formulated.

The Meeting proper commenced on Tuesday, July 26th, with the masterly Address by the President, SIR FARQUHAR BUZZARD, entitled "And the future", which appears in full in the *British Medical Journal* of July 25th.

The numerous Sections met in the University Museum and were well attended. I could be present only at those of Medicine, and Pharma-

cology and Therapeutics, and hence can only speak of the work done there.

The Section of Medicine.—The whole of the first morning was devoted to a consideration of "The treatment of chronic rheumatism, articular and non-articular." Dr. Tidy, of London, opened the discussion by saying that he regarded rheumatoid arthritis, osteo-arthritis and fibrositis as all coming under the term "chronic rheumatism". A septic focus should be looked for, and only when such was definitely present was vaccine therapy justified. The only drug that had any specific action here was gold, but its use required great care. Schemes of dieting had their chief action in alteration of weight. He did not think that thyroid extract had any specific effect. In the acute stage absolute rest was necessary, and a single daily movement of each affected joint should be instituted, to lessen deformities and adhesions. During the rest of the time splints were required. Heat in various forms was of great value. He was sceptical of the special effects claimed for the various spas except as regards the external use of waters. All physical and balneo-therapy should be directed by a medical practitioner.

Dr. ABERCROMBIE, of Sheffield, thought that the psychological element was important. The confidence of the patient should be reinforced.

Dr. BUCKLEY, of Buxton, regarded the pro-

of great importance, and we should listen to the patient's own description of his sensations with great care, for from it we could often come near to a complete diagnosis of the underlying cause. Gastric flatulence might be odourless or foul; the former usually being due to aerophagy and the latter to some organic trouble.

Dr. J. M. H. CAMPBELL, of Oxford, considered cases of acute indigestion occurring at night and with no history of previous gastric trouble as often being cases of coronary thrombosis. Many patients with this serious trouble were treated for indigestion.

Dr. THOMAS HUNT pointed out how often intestinal (and colonic) conditions caused epigastric discomfort. The sense of fulness often felt by people after a very small meal was due to a failure of the normal gastric relaxation.

Dr. A. F. HURST discussed the mechanism of aerography, and considered that many cases of epigastric discomfort were due to gaseous distension of the splenic flexure of the colon. This might be relieved by reducing the starch content of the diet. An abnormal valvular mechanism at the cardia may cause the condition of "air-lock" in the stomach.

Dr. JOHN PARKINSON was often impressed by the absence of the complaint of "wind" where this might be expected from the distension of the stomach seen with the x-ray. Pain in the

or less normal and the weight stationary or increasing. Blood sedimentation gives some information about the development of resistance, and serial examinations of the blood picture, the leucocytes being counted by the Arneith or Schilling methods, even more. The theory of relaxing the tension and so allowing the cavity to contract has greatly modified the technique of procedure. Our object should be not to completely collapse the lung, much less to compress it, but to relieve local tension in the diseased area, while allowing the healthy portions of the lung to function. A pneumothorax, when large, tends to compress the healthy parts, which is not what is required. What we want is "selective relaxation". This is usually best done by division of adhesions, but where this fails more radical attacks on the chest wall may be required. In rare cases apicolysis is of value. The speaker strongly condemned evulsion of the phrenic nerve which paralyzes the diaphragm and thus reduces the function of the lower part of the lung, which is usually not the site of the cavity.

DR. F. G. CHANDLER, of London, agreed that phrenic evulsion was seldom advisable. He thought that oleothorax was often useful, especially where obliterative pleurisy was occurring.

DR. W. ANDERSON, of Aberdeen, while admitting that relaxation of the lung was the chief cause of improvement following various surgical procedures thought that other factors, such as rest, accounted for much of the benefit.

DR. GEOFFREY MARSHALL, London, believed that division of long narrow adhesions was important when the patient had improved and the cavity could not be seen with the x-ray. Otherwise such cases were often disappointing later on.

DR. C. PRICE THOMAS, Newbridge, expressed the opinion that too many physicians still relied upon rest and so-called "building-up" therapy. He agreed that division of the adhesions with the cautery should be more often performed. Sometimes contralateral artificial pneumothorax made a cavity larger, due probably to a valve-like obstruction of the bronchus draining it.

MR. HUGH REID and MR. J. B. HUNTER, both of London, claimed that phrenic evulsion should not be too much condemned. It had its uses in carefully selected cases.

DR. GRAVESEN, in closing the discussion, said that there was still a great deal of activity in a collapsed lung. In his opinion phrenic evulsion was a useless procedure.

The Section of Pharmacology, Therapeutics and Anaesthesia.—The first session was a combined one with the Sections of Physiology and Biochemistry and Pathology and Anatomy, and consisted in various laboratory demonstrations. Many of the methods were of purely scientific interest but several had a practical bearing. Several useful pieces of apparatus were shown

for the easy administration of oxygen, and Drs. MARRIOTT and KEKWICK demonstrated a simple mechanism for the slow transfusion of large quantities of blood by the "drip" method. Drs. CARLETON and LIDDELL, of Oxford, exhibited cats in which the exteriorized artery was available for taking blood pressure. "A meat diet produced a placid animal with a low blood pressure; milk, a hungry animal with a high blood pressure". This unlooked-for result shows how careful we must be in applying animal experimental results to man.

The second session was devoted to the discussion of "Cyclopropane anaesthesia" in the first place, and then went on to discuss "Anaesthetics in labour". During the whole session the Section combined with that of Obstetrics and Gynaecology.

DR. RALPH WATERS, Madison, U.S.A., opened the discussion on cyclopropane by suggesting a new process of manufacture of the gas which much reduced the cost. This anaesthetic caused no respiratory stimulation, but on the contrary a slight depression. The pulse should be carefully watched because there was a risk of ventricular fibrillation. This was apt to be preceded by a very slow heart. The post-operative respiratory complications were definitely less than with other anaesthetics. The use of the drug was still in the experimental stage and much has yet to be learned about it.

DR. DIVINE, of Hull, in an experience with 92 cases, said that he had seen both bradycardia and arrhythmia under its use.

DR. SIMMONS, Bournemouth, recorded a death from its use in which ventricular fibrillation was noted. Several other speakers gave their experience with the gas which was far from encouraging.

The discussion on "Anaesthetics in labour" brought out many differences of opinion, both as to the drugs to be used and as to the time and the methods of employing them.

MR. L. C. RIVETT said that two trained persons should always be present at every labour.—surely a counsel of perfection!

DR. FEATHERSTONE, of Birmingham, remarked that if the patient was to be rendered unconscious (*i.e.*, anaesthesia induced) then this should be done by one practitioner, leaving the other free for necessary manipulations. Most speakers thought that chloroform was on the whole the best anaesthetic during labour, but should not be used too early. According to Dr. HELEN E. RODWAY it was unwise to use any drugs for the relief of pain until the uterine contractions were well established, and inhalation anaesthesia should be reserved for the second stage.

DR. R. J. MINNITT, Liverpool, called attention to the difference between analgesia and anaesthesia, and believed that the former is all that is usually necessary.

DR. Z. MENNELL, the final speaker in the symposium, was in favour of the proper use of chloroform both as an analgesic and as an anæsthetic.

The social part of the gatherings of the British Medical Association is always a strong feature and the Oxford meeting excelled itself in this respect. There were many lunches and dinners, receptions and garden parties. Even special breakfasts were held on several mornings. There was much dancing and golf for the active, and a chess tournament had been planned but no time could be spared for it. One particularly enjoyable garden party was given by Mr. H. S. SOUTTAR for those who had been overseas to the Melbourne meeting. DR. DOUGLAS, the oldest member of our party, was there and was congratulated on being elected a vice-president of the Association.

LORD NUFFIELD had several parties out to see the Morris car works, and we there saw the marvellous way in which these cars were assembled and turned out at the rate of 500 a day.

Of Oxford I will say little, as it is so well

known. The town reeks of antiquity, and yet in many ways is thoroughly up-to-date. Mr. SOUTTAR's house is over four hundred years old.

On one evening the mayor held a reception in the Town Hall. The mayor is a lady, COUNCILLOR Mrs. TOWNSEND, and very well she discharges her duties, and at the annual banquet made a charming speech. In many English towns and cities, as in Oxford, the Councillors are the lower rank of city fathers, and the aldermen the higher, and the latter hold their appointments for life, while the Councillors are elected every three or four years. The mayor is appointed annually.

On Friday evening Dr. R. R. MARETT gave the annual popular lecture, which was largely attended. His subject was "Antimicrobiology and medicine", and he spoke in the old Sheldonian Theatre.

On Saturday there were several garden parties, but most of the members had scattered to their homes, all doubtless bearing away with them many happy memories of a most successful meeting and probably having the best of intentions of meeting again in Belfast next July.

Men and Books

THE DAWN OF TROPICAL MEDICINE*

BEING A BRIEF ACCOUNT OF THE LIFE AND
WORK OF SIR PATRICK MANSON

BY P. MANSON-BAHR, D.S.O., M.D.,
F.R.C.P., D.T.M. & H.

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No attempt is made here to claim that Manson discovered Tropical Medicine, but emphasis must be laid on the fact that by his work and precepts he made it a new and living thing; that he was the first to elucidate the cause and transference of many hitherto obscure tropical diseases; that as a great clinician he transformed the specific treatment of these diseases; and that, most certainly, he was the first to found and direct a school devoted to the teaching of tropical medicine and thereby to render safe for colonization and development many unhealthy and inhospitable countries in the British Empire and other parts of the tropics. Indeed the benign influence of his discoveries, of his example and of his life, is world-wide.

Of pure Scotch parentage, though descended originally, as he often jocularly remarked, from Norwegian pirates, Manson was born in humble

circumstances in the ancient town of Old Meldrum, Aberdeenshire, on the 3rd October, 1844. His earlier years were spent in training at the gymnasium of Aberdeen city for the engineering profession, a training which in originality of method and dexterity in execution afterwards stood him in good stead. However, the Fates ruled otherwise, for, at the early age of sixteen, he developed a curvature of the spine for which he had to rest for six months and it was during this period that he decided to enter the medical profession. Neither at school nor at the university did he display any particular brilliancy, but he was a steady hard-working student. He, however, made such headway that by the age of twenty, in 1864, he had passed his final examinations. In 1865 he held the position of Medical Officer to the Durham Lunatic Asylum, making a series of careful dissections of the brains of the insane, and he published an article on minute aneurysmal dilatations of the cerebral arteries which he maintained were the cause of mental disease. In 1866 he "fared foreign", and in the autumn of that year landed at Takao on the southern shores of Formosa, where he spent the next four years. In 1870 he moved to Amoy, a "treaty port" on the mainland of China in the Bay of Hiu Tau, where he worked more or less in obscurity till 1875.

Amoy was typical of a Chinese city in those days — unsanitary, ill-kempt and filthy — just teeming with disease, and here he was led to reflect upon the causation of elephantiasis and leprosy, the two diseases which he mostly en-

* An address (somewhat abbreviated) delivered at the opening of the 90th course of study at The London School of Hygiene and Tropical Medicine on February 3, 1931.

countered. It is certain that from his peculiar sympathy with the Chinaman, his professional skill, and outstanding personality, he soon gained a moral ascendancy with the people with whom he was brought into contact, to such an extent that he gained their confidence, and was able to perform operations hitherto unheard of in China. We know from his records that in one year he removed with complete success "a ton of elephantoid tissue", besides performing the operation of "cutting for stone", and many upon the eye. Very soon his reputation for surgery, and especially his knowledge of eye diseases, resounded all over China. In midwifery he appears to have been no less successful, and to those familiar with the conservative disposition of the Chinese this in itself is very remarkable.

Returning to England in 1875, he busied himself in museums, medical schools and libraries, endeavouring to find out more about the diseases in which he was so deeply interested, but he could find little literature and no authorities on the subject and his enthusiasm received no encouragement. At last one day, in the autumn of 1875, he found amidst the dusty precincts of the reading room of the British Museum the writings of one Timothy Lewis, a very distinguished officer of the Army Medical Service in India. In 1870 this Lewis had discovered certain nematode worms in the blood of natives of Calcutta which he had named the *Filaria sanguinis hominis*—the threadworm of the blood of man. Manson instantly seized upon the idea that these worms might be the cause of elephantiasis, as well as of many other diseases he had observed in Amoy.

The close of 1875 saw him returning to China, provided with a wife and a compound microscope, and fired with many new ideas. Immediately on arrival he set to work to look for the *Filaria* amongst the blood of his Chinese patients in his primitive hospital, which was a rough two-storied Chinese house in Amoy. To aid him in his researches he enlisted the services of two local Chinese assistants, and he soon noted that the more assiduous and the one who worked in the hospital wards late at night was successful in bringing him slides containing the microscopic parasites. A lesser man, or one endowed with a less enquiring mind, might not have noted this discrepancy, but it instantly occurred to him whether this fortuitous occurrence might not be due to the entry of the *Filaria* into the bloodstream at night time only; and so it proved to be, for after six weeks' intensive study on one Chinaman (Huito, who should go down to fame) he discovered that his suspicions were indeed correct. The worms appeared in the blood at night time only, but disappeared completely during the hours of daylight. This was indeed a puzzling fact, and when, in 1877, his researches were related at a meeting of the Linnæan Society of London, one sceptic present wished to know whether nature had provided the blood filariæ "with watches". Later it was discovered that

when the habits of the patient were reversed, those of his parasite followed suit. So that by sleeping in the daytime and remaining awake at night the filariæ could be found in swarms in the day blood, but not at night. On making minute observations upon the filariæ removed from the blood and studied under the microscope, Manson had little difficulty in concluding from their structure that they were embryos or the immature state of a much bigger parent worm which, he concluded, must inhabit some tissues of the human body.

This was proved to be true in December, 1876, when Bancroft, in Brisbane, Australia, discovered the adult worm—a long filamentous hair-like creature—almost two inches in length, which inhabited, as male and female individuals, the lymphatic tissues. Now Manson's blood filaria was a much smaller creature, only 1/80th of an inch in length; it was encased, he found, in a loose sheath, in which it struggled aimlessly—tied down as it were, like a man in a sack. The embryo itself had no organs of alimentation, being neither provided with a mouth, an anal pore, or a digestive canal. It seemed to him that nature had provided this small creature with a sheath for some special purpose, for when the blood was cooled outside the body the minute filaria was seen to rupture through its sheath and swim rapidly about in the blood like an active eel. He argued too that the embryos could not possibly develop to any further stage in the blood in which they were being swept along like so many inanimate objects—for did they do so in such countless millions—then the human host himself, like Herod of old, would be entirely "eaten of worms". So he argued that some agent must be necessary for the transference of the filaria from one human being to another and for the development of the parasite outside the human body. It must be a winged agent—something that was nurtured on human blood and something that fed at night time only. What other could that be than a mosquito?

Now the common brown mosquito of Amoy bit at night time only, and was very numerous in the native quarters. So in August, 1877, Manson induced Huito—his filaria-infected Chinaman—to sleep in a mosquito cage and to allow himself to be freely bitten by those insects. The next morning the insects were collected in separately labelled bottles, when engorged with blood, and were kept alive as long as possible. It was not possible to do so for longer than five days, and by dissecting them at frequent intervals with such a primitive instrument as a pen-point Manson soon realized that he had "stumbled upon an important fact with a distinct bearing upon human pathology". For he witnessed a most remarkable fact—the migration of the embryo-filaria, having cast its sheath in the stomach contents, through the walls of the viscus into the muscles of the wings where it developed rapidly into a much larger worm-like creature. "I followed it up," he says, "as best I could with

the meagre appliances at my disposal, after many months of work, often following up false scents, and ultimately succeeded in tracing the filaria through the stomach wall into the abdominal cavity and then into the thoracic muscles of the mosquito. Manifestly it was on the road to a new human host." The idea that a winged insect was the disseminator of disease germs, and that it was an essential link in the development of these parasites, without whose agency it would cease entirely to exist, was a new and startling fact in medicine and, in fact, in biology.

In August, 1878, Manson's paper on the development of the *Filaria sanguinis hominis* and on the mosquito, considered as a nurse, was published in the *Transactions of the Linnæan Society of London* and was received with consternation, tinged with scepticism. It proved to be the corner-stone of what is now known as Tropical Medicine, and henceforward Manson had every right to be regarded as a famous man; but in his modesty—for with all his greatness Manson was essentially modest—we find him writing to Cobbold, the greatest extant authority on these matters—"Men like myself in general practice are but poor and slow investigators, crippled as we are with the necessity of making our daily bread."

One of the greatest stumbling blocks to the advancement of knowledge in China was the very great difficulty, or impossibility, of examining the body after death. Only twice did Manson, at great personal risk, undertake this disagreeable but essential task. In both instances he made remarkable discoveries. In the first he found the adult *Filaria bancrofti*, thus confirming Bancroft's original discovery, and on the second occasion he found some ribbon-like worms which proved new to science, and have since been proved to be the immature stages of a big tapeworm. Being denied the opportunity of necropsies in man, he had recourse to dogs, cats and birds of various kinds. In these he discovered a whole host of new parasites, many of them blood worms like the filaria of man, from which he deduced important facts concerning their habitat and mode of life, and which he applied to the parasites of man.

One day a Chinese mandarin entered his room and very rudely and insultingly spat on the floor. "My indignation," says Manson, "evaporated on seeing that the sputum was tinged with blood". So, seizing some with the forceps he immediately placed it under the microscope, and there he recognized the eggs of a strange and hitherto undiscovered worm. It turned out to be the lung fluke—*Paragonimus*—the extraordinary life-history of which he afterwards helped to elucidate. For we know that the eggs of this fluke hatch in water into a motile creature which first enters a fresh water snail and then a fresh water crab in order to get back once more into the lungs of man!

About this time too Manson discovered quite independently, almost simultaneously with Hansen (1879), the leprosy bacillus which he expressed

from leprous juice. It must be remembered that when summing up the remarkable discoveries that he was working absolutely isolated from contact with other scientists or authorities and cut off from museums and libraries. The idea of this isolation, which must be felt to be realized, makes his achievements all the more remarkable.

In 1889 Manson retired to Scotland. He had amassed considerable wealth, and after twenty-three years in China he had become a famous man, and felt disposed to disport himself in the bounteous woods and waters of his native Aberdeenshire. However, within a year, owing to family misfortunes and the disappreciation of the Chinese dollar which occurred at this moment, he was compelled to try his luck as a consultant in London. Thither he repaired to live many lean and, from the material sense, unprofitable years at 21 Queen Anne Street, Cavendish Square. But soon he found fresh fields for exploration. In blood specimens sent to him from various tropical countries he found no less than four new blood filaria in man—one of which from West Africa—*Filaria loa*—proved the absolute antithesis of his original *Filaria bancrofti*, in that it appeared in the blood stream in day time only, disappearing in the hours of night. His hypothesis, founded on native tradition, that it was carried by a day-biting "mangrove fly" was proved to be correct nearly 24 years afterwards. Here in a small room at the top of the house, euphoniouly dubbed the "muck room", he worked out the life history of the guinea worm in the water flea (*Cyclops*), made frequent observations on many other parasites, and predicted their life history in every ease, almost with prophetic accuracy. This small room proved to be the nucleus of the future London School of Tropical Medicine. In 1892 Manson made a great step forward in the medical life of London, for he became physician to the Seamen's Hospital Society, a position which gave him ample material for study and practice in the hospitals in the London Docks, under the service of this great Corporation. Here he first began to work seriously with the malaria parasite. By means of a new stain (borax methylene blue) of his own composition, he was able to advance knowledge of the minute structure of this microorganism beyond any hitherto known. He watched the antics of this parasite in blood withdrawn from the body in much the same way as he had observed the filaria in China almost twenty years before. From these pregnant observations, which have never since been seriously challenged, he was able to make suggestive hypotheses upon the dissemination of this disease—"Malaria—bad air—which has so far been popularly ascribed to *miasmata* or emanations from the marshes". So that, in December, 1894, he was able to summarize his knowledge and to publish what is known as *Manson's Malaria-Mosquito Theory*. Briefly this theory compared the life story of the filaria parasite to the supposed life history of the malaria organism, and demanded that a stage

outside the human blood must be passed within the body of a special kind of mosquito found in those tropical countries where malaria abounded. Manson himself approached the Royal Society for a modest grant of £300, to enable him to proceed to British Guiana to work out his project there, which he could not do with very limited material in the cold and dusty atmosphere of his "muck room". Shame be it said that this request was refused! Earlier in that year he had become acquainted with Surgeon-Major Ronald Ross, who had returned from India, where he had interested himself in malaria and had written several papers on the subject. But Ross had not recognized the malaria parasite under the microscope and this, as well as much other technique which he had mastered, Manson set out to teach him.

In 1895 Ross returned to India, inspired by Manson's hypothesis and precepts, and supported by Manson's great authority with the government in England. The years 1895-1899 constituted a period of great activity in malaria research. In this then two great men were closely associated. Indeed there has never been such a close scientific collaboration, and it culminated, as all the world now knows, in the complete vindication of the theory of "Mosquito Manson", as he was then known, worked out to finality by the undying enthusiasm, persistence, ingenuity and zeal of Ronald Ross. Thus did Manson in the last days of the last century come into his own and received the long-deferred honour of the Fellowship of the Royal Society; that was the award of the master—that of the pupil, a similar fellowship and the Nobel Prize. History, however, will record its judgment, that without the initial and basic spade work of Manson's filaria days there would have been no mosquito-malaria theory, and we should still have been looking for the malaria parasite, as Ross so incisively puts it, in water or in air!

On April 9, 1922, Manson died. What is one to say of a great life like his? He was alone in his field, was the great original thinker of his time in the special department of medicine. He died full of honours. Greatly distinguished in his career, a lover of children and of animals, honoured as an oracle in the school of his own foundation, appreciative of sport and good literature, Manson belongs to the company of those who have "warmed both hands before the Fire of Life". Without Manson, and without his wonderful prophetic hypotheses, it is safe to say that the elucidation of the mystery of yellow fever would have been long delayed, and that no Gorgas would have arisen betimes to guide American energy, wealth and labour to construct that world-marvel of enterprise, the Panama Canal, and no one, it is safe to say, was more appreciative of the part played by Manson than General Gorgas himself.

In scientific work what better maxim could be followed than the precepts laid down by Manson himself:—

"Never refuse to see what you don't want to see, or what may go against your own cherished hypotheses, or against the views of authorities. These are just the clues to follow up, as is also, and emphatically so, the thing you have never heard of or seen before. The thing you cannot get a pigeon-hole for is the finger-point showing the way to discovery."

THE SEARCH FOR THE WESTERN SEA*

A REVIEW

By ALBERT G. NICHOLLS,

Montreal

"The Call of the West" has been from the beginning a vital factor in the exploration of America. Mr. Burpee styles it "The spirit of adventure of a vigorous people acting upon a deep-rooted racial tendency to follow the path of the Sun". A thousand years ago the Northmen heard the call and responded to it, thereby discovering a new continent. Nearly four and a half centuries later America was rediscovered, by Columbus, and from that time onward we have the enthralling tales of exploration associated with the names of the Cabots, Verrazano, Cartier, Hudson, Button, Foxe, Mackenzie and Fraser, to name only some. To find the Western Sea, the pathway to golden Cathay, was the dream of the early British and French explorers; the story of their quest is a golden epic. "The Search for the Western Sea" is the keynote of exploration in northwestern America, and so provides an appropriate title for our author's fascinating story.

It is a remarkable fact which "may not be without significance, that from beginning to end, from Hudson and Cartier to Mackenzie and Fraser, the men who were engaged in this long search for the Western Sea were for the most part men of Brittany and Normandy, of Scotland and the coast towns of England, legitimate descendants of those hardy Vikings who first of white men set foot on American soil". It is also not without fitness that the expedition that first succeeded in reaching the shore of the Pacific overland consisted of a party of French-Canadian *voyageurs* under the leadership of a Scottish-Canadian.

Mr. Lawrence J. Burpee, is one of the best known of Canadian litterateurs. He has been for twenty-five years Secretary for Canada of the International Joint Commission. He organized and was for several years president of the Canadian Historical Association. He has also been president of the Canadian Authors' Association. He is the editor of the *Journal of the Canadian Geographical Society*. He has been awarded medals by the Royal Society of Canada

* "The Search for the Western Sea: the Story of the Exploration of Northwestern America." Lawrence J. Burpee. Two volumes; 1,609 pp.; illustrated. New and revised edition. Price, \$10.00. On sale at Dora Hood's Book Room, 720 Spadina Avenue, Toronto.

and the French Academy for his outstanding work in Canadian historical research. He is the president of the Royal Society of Canada. There can, therefore, be no question as to his competence for the task he has undertaken.

"The Search for the Western Sea" was first published in 1908 and at once established itself as the authority on the exploration of north-western America. This first edition is now rare and expensive. Since this date much new matter has come to hand through the researches of many scholars, and documents acquired since by the Dominion Archives have thrown new light on the character and achievements of the early explorers in Canada. The present volumes, therefore, can be accepted as a great advance on the original work.

Mr. Burpee gives some space to the pioneer discoverers, Leif Ericson, Columbus, Verrazano, the Cabots, and Jacques Cartier, but expends his talents on the more modern period, on such men as Hudson, James, Hearne, La Vérendrye and his sons, on Carver, Pond, Mackenzie, Simon Fraser and David Thompson. His narrative practically closes with Mackenzie's overland expedition to the Pacific, Fraser's descent of the Fraser River, and Thompson's exploration of the Columbia, the accounts of these being graphically told. The hitherto uninitiated reader will find it a little complicated to follow the innumerable geographical details of the story, but the subject is much clarified by the presence of an excellent introduction.

Western and northwestern Canada is studded with countless lakes and intersected by many winding rivers. By means of portages the early explorers, aided or hindered, as the case might be, by the reports and activities of the Indians, eventually made their way southward, northward, and westward by the waterways, but the going was hard and tedious, as the rivers were often long and tumultuous. One wonders at the learning and patience of our author which have enabled him to present the intricate matter of the geography of this part of Canada and its bearing on the travels of the pioneer explorers in such a clear way. The task was great; it has been admirably performed. Details which might have proved boring are lightened by anecdote, personal sketches of the actors in the drama, and accounts of the various Indian tribes with whom the wanderers came in contact. The result is a gripping and informative tale.

The subject is dealt with systematically under three headings—"The Northern Gateway", "The Southern Gateway", and "The Road to the Sea".

The northern gateway is Hudson Bay. In this section of the book we have an account of the discovery of Hudson Strait (by an unknown before 1508), by the Portuguese (?1558 to 1570), and by Davis (1587), and a fuller account of Hudson's voyage, with its disastrous ending. The search for the "Northwest Passage", how-

ever, still continued, and we learn about the expeditions of Sir Thomas Button, Jens Munk, and Captains Luke Foxe and Thomas James. We are informed of the interesting fact that the "Strange and Dangerous Voyage" of Captain James formed one of the main sources, if not the main source, of Coleridge's "Ancient Mariner". Then follows the first voyage of Chouart and Gillam on the *Nonsuch* in 1668, on behalf of a group of men who two years later formed themselves into The Company of Adventurers of England trading into Hudson's Bay, commonly called the Hudson's Bay Company. On this occasion Chouart and Gillam established Fort Charles on James Bay, the first trading post of the Company, and thus initiated an enterprise that has flourished up to the present day.

Next comes the story of the first authenticated journey from Hudson Bay to the upper Saskatchewan River—that of Anthony Hendry (1754-55), which is followed by a graphic account of Hearne's discovery of the Coppermine, the massacre of the Eskimos at Bloody Falls, and the surrender of Fort Prince of Wales to Admiral LaPerouse under circumstances favouring of opera bouffe. The chapter closes with the names of Philip Turnor, Peter Fidler and David Thompson. Hearne's travels are important as they settled finally in the negative the question as to whether there was or was not a "Northwest Passage" by way of Hudson Bay.

If the northern gateway was preeminently the portal by which the English adventurers entered the unknown land, the southern gateway, that by way of the St. Lawrence valley and the Great Lakes, was equally associated with the French. Two hundred years of exploration had opened up this tract of country as far west as the height of land that separates the waters flowing east to the Gulf of St. Lawrence from those that flow north of Hudson Bay and south to the Gulf of Mexico. Burpee credits Radisson and Chouart with being the first to connect Lake Superior with Hudson Bay by an overland expedition (1662). The great heroes in the epic are Pierre Gaultier de La Vérendrye and his three sons. In the face of much opposition and adverse circumstances these heroic men discovered Lakes Winnipeg, Manitoba, Winnipegosis, some of the upper reaches of the Saskatchewan River, and traced the Missouri as far as the foot-hills of the Rocky Mountains (about 1743). After the conquest of Canada numerous attempts were made by the English to realize the dream of the French, to blaze a trail to the Western Sea, the first of which was that of Jonathan Carver (1766-68) who left an account of his wanderings in his "Travels through the Interior Parts of North America", an entertaining though somewhat untrustworthy production.

The second volume is, if possible, more delightful than the first. In it we have the fruition of the hopes of the long line of intrepid explorers who brought honour to the French and English races. The Western Sea is discovered by path-

ways from the east. We learn something of the operations of that second great trading concern, the North-West Company, which had its headquarters in Montreal and became such a formidable competitor of the older Hudson's Bay Company. The rivalry between the two became intense, finally culminating in bloodshed. Then, commonsense prevailed and the two companies amalgamated. We are brought face to face with James Finlay, of Montreal, who, not later than 1767, reached the Saskatchewan, and with Alexander Henry the elder, who in 1775 reached the Grand Portage, Lake Winnipeg, Saskatchewan River, and Ile à la Crosse. Other noted figures of the time are Peter Pond, Joseph and Thomas Frobisher, Roderick Mackenzie, C. J. B. Chaboillez, and Simon McTavish.

The remarkable travels of Alexander Mackenzie, Simon Fraser and David Thompson are dealt with at length and form the most dramatic portion of the book. The resourcefulness, skill and determination of these great men are almost unbelievable. Posterity owes them much.

Mackenzie discovered the mouth of the great river named after him, tracing various sections of its course at different times, and eventually stood at one of its remote sources two thousand four hundred and twenty miles up stream. He was the first of the overland explorers to stand on the shores of the Pacific. He travelled up the Peace River, up its tributary, the Parnip, and by a portage and some intervening waters reached the Fraser River, emerging at the sea somewhere near the present Bella Coola. This was in 1793.

Simon Fraser discovered the Fraser River and descended it almost to its mouth, reaching a point near where the city of New Westminster now stands. Fraser at the time thought he was on the Columbia River and Thompson was paddling up the Columbia without realizing it. This was not surprising!

Thompson reached the source of this river in Upper Columbia Lake in 1808, and in about three years had traced its course from source to mouth, a distance of eleven hundred and fifty miles. Dr. Coues pays Thompson this fine tribute—"The world can never be allowed to forget the discoverer of the sources of the Columbia, the first white man who ever voyaged on the upper reaches and main upper tributaries of that mighty river, the path-finder of more than one way across the Continental Divide from Saskatchewan and Athabaskan to Columbian waters, the greatest geographer of his day in British America, and maker of what was then by far its greatest map." Thompson, we understand, has also another title to fame worthy of note, in that he was the surveyor who laid out the principal streets of Montreal. In his old age he fell on evil days, dying in poverty on February 16th, 1857, at the age of nearly eighty-seven years. Three months later his wife followed him. They are buried

in Mount Royal Cemetery, Montreal. The book closes with an appreciative account of the many notable men connected with the Geological Survey of Canada whose work has done so much to fill in the gaps in the geographical record left by their predecessors—Robert Bell, George M. Dawson, A. P. Bell, the Tyrrells, and others who might be mentioned. Even yet much remains to be done, but the aeroplane is with us, and surveys and observations can now be made in days, where formerly they took years.

We could have wished to get more information on medical topics, but, no doubt, these had no special interest for Mr. Burpee. We wonder whether the various explorers in our Canadian North-west had medical men with them. Possibly the early expeditions by ship into Hudson Bay had their doctors, but we are not told. The French sometimes took medical men along with them. We know, for instance, that LaSalle, when he went on his famous voyage down the Mississippi (1678-83), had two with him—Jean Michel and Jean Roucel.

There are sundry statements which lead us to infer that scurvy took the usual toll that was so exacting in those early days. The white men were, on one occasion at least, specifically blamed by the Indians for introducing smallpox.

An interesting anecdote is told on page 485 in which Alexander Mackenzie figures. The son of the old chief of the Coast Indians was suffering from an ulcer. The white chief was requested to touch the sick man and make him well. This was somewhat disconcerting, and Mackenzie had recourse to an old stand-by—Turlington's Balsam. The effects not being immediately apparent the native doctors again took charge. They blew on the unhappy patient and then whistled; they rubbed him violently on the stomach; they thrust their fingers into his mouth, and spouted water into his face. He was then carried on a plank into the woods, where a fire was kindled, and the ulcer was treated heroically by cauterization with red hot instruments. We are told that the scene was too much for Mackenzie, who hastily withdrew.

There is an interesting reference to Dr. John Coakley Lettsom, the celebrated Quaker physician who founded the Medical Society of London (1773), and in whose memory the Lettsomian Lectures were instituted. The "Travels" of Jonathan Carver, according to Professor Bourne, "can no longer be ranked as an authentic record of the observations of the supposed author", and he conjectures that in its present form this record is the work of Lettsom, who wrote much and was the charitable friend of Carver. It is assumed that Lettsom prepared the book from Carver's notes and recollections of his journey, and padded it out with unacknowledged extracts from French journals and histories of New France. Commenting on this, Burpee adds,—“Admitting the

correctness of Professor Bourne's conclusions, it is singular that a book so cobbled together could have inspired two such masterpieces as Chateaubriand's 'Voyage en Amérique' and Schiller's 'Nadwessiers Todtenlied', later translated by Bulwer-Lytton as 'The Indian Death-Dirge.'

This imperfect sketch will give some indication of the character of Mr. Burpee's book. Those who take an interest in the early exploration of our country will find in it a rare treat.

Hospital Service Department Notes

Major and Minor Operations

Enquiries are frequently made as to how these two groups can be differentiated and a perusal of the literature makes it soon evident that definitions differ widely. For instance, the description of a major operation as one that involves the risk of a life might require almost all operations to be considered as major ones, for, in almost all, when done under certain circumstances, there is possible danger to life. In an illuminating discussion of this subject, the Editor of the *Canadian Hospital Journal* reviews various attempts to clarify this differentiation.

A definition given by the American Medical Association considers as major "surgery within the cranial, thoracic or abdominal cavity, or any surgery which, through the nature of the operation or the anæsthetic demanded, may carry a distinct menace to life". Dr. S. S. Goldwater, of New York, states that "a major operation is a severe or serious operation, not a slight or trivial one, but from comparatively trivial surgical procedures serious consequences sometimes result. The test lies in the gravity of the operation, which must be gauged not merely by the technical difficulty of the procedure but by the risk to the patient . . . Elements to be considered are—the scope of the surgical procedure; the danger of shock; the presence of known complications; the probability or possibility of unsuspected pre-existing surgical complications; the probability and possibility of post-operative complications; the probable duration of the operation; the age and general condition of the patient; the degree of mutilation; the amount of pain or mental anguish caused; the nature of the anæsthetic; and the risk of legal complications in the case of an unsuccessful result."

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

Dr. M. T. MacEachern, of the American College of Surgeons, has stated that "the best definition . . . is that which we received from the American Medical Association, which states that a major operation is a surgical procedure that entails immediate serious consequences to the patient and requires skill and training to perform". Dr. Nathaniel W. Faxon, of Boston, who, like the two authorities quoted above is also a former president of the American Hospital Association, after reviewing various factors, says "The most important factors in defining major and minor surgery are: "Whether the patient remains ambulatory, whether a general anæsthetic has been given and the risk for the patient". He points out that many infections of the hand, formerly regarded as of a minor nature, are now considered as requiring major procedures because of the economic value of a functioning hand.

In summing up the various opinions the Editor notes that the differentiation is usually based upon factors associated with the patient, and makes the suggestion that certain simplification would be forthcoming if the *skill of the surgeon* were made the deciding factor, as an operation may be minor when done by a skilled surgeon but would be of major nature, because highly dangerous to the patient, if performed by an inexperienced or ill-trained surgeon. Reference is made to the procedure in one well-organized hospital where a full list of operations is divided on the basis of the rank of the surgeon who may do them. For instance, brain surgery, open bone work, gastric and gall-bladder surgery, all internal malignant conditions, splenectomy and post-operative herniotomies *inter alia* may be done only by the senior major surgeon; empyema, rib-resections, trachelorrhaphy, non-ruptured appendicectomies and inguinal herniotomies, among others, may be done by the junior major surgeon; the latter may only do benign breast tumours, umbilical hernias, uterine suspensions or ovarian cysts, after consultation with the senior major surgeon. The minor surgeon may do tonsillectomies, transfusions, diagnostic biopsies, finger and toe amputations, emergency tendon- and nerve-suturing, and other listed and obviously minor procedures.

This basis has the advantage of giving the patient assurance of competence on the part of the surgeon officiating. From a practical viewpoint one questions to what extent it could be adopted by our hospital staffs. In highly organized and departmentalized hospitals there should be very little difficulty, particularly with reference to ward or staff patients, but in the majority of our hospitals (and there are more under fifty beds capacity than over) the surgical work is done by a small handful of men, all of whom are usually in general practice as well and

usually on an equal footing in the hospital organization. In such smaller institutions it would be difficult for the staff to determine to what extent each of the local surgeons would operate. However, no matter how small the hospital (excepting perhaps isolated one-doctor hospitals) the staff could readily adopt the suggestion of listing certain operations which they would mutually agree would not be attempted (barring emergency situations) except after consultation and with certain qualified assistance.

Provincial Association Notes

The Nova Scotia Medical Society

Reiterating its approval of unification of the Canadian Medical Association with the provincial societies, the Nova Scotia Medical Society met in annual conclave at Halifax, August 31st to September 5th. The meeting was concurrent with the Dalhousie Refresher Course which took care of the scientific part of the program. The business sessions of the society were well attended and registration the largest in many years.

Outstanding at the first meeting was the report of the special committee appointed to consider amalgamation with the Canadian Medical Association. The report warmly approved of the motive and principle of unification. It was felt that the problem was a great one and that every step should be carefully planned and checked in advance. It was further pointed out that the Nova Scotia Medical Society is under special charter of the Nova Scotia government and is not free to dissolve itself or alter its status. The report recommended further investigation of the plan and cooperation with it, and advised consultation with the department of the Provincial Attorney General. The report was adopted.

Dr. K. M. Robertson, President of the Canadian Association, and Dr. T. C. Routley were welcome guests at the banquet and meetings where they spoke on the work of the Association.

Sterilization of the mentally unfit was the problem which Dr. R. M. Benvie, retiring president of the society, served with the coffee at the annual banquet. Dr. Benvie, who occupied the chair with justice and grace throughout the sessions, gave a presidential address which gratified both those who sought learning and entertainment. Presenting the modern conception of embryology with reference to inherited characteristics, he established reasons for the increase of mental defectives in Canada. They cost the people of Canada twelve

million dollars yearly, nor is this the most serious aspect of the tragedy. It would take three thousand years to reduce the incidence, by sterilization, to one per thousand. This, Dr. Benvie felt, was good reason for the immediate legalizing of sterilization. He urged on the profession the importance of preaching the doctrines of eugenics and heredity to the laity.

Dr. J. R. Corston, of Halifax, was elected *President* for 1936-37. *First Vice-president*, Dr. A. Calder, Glace Bay; *Second Vice-president*, Dr. J. H. L. Simpson, Spring Hill; *Secretary*, Dr. H. G. Grant, Halifax; *Treasurer*, Dr. W. L. Muir, Halifax. Study committee on confederation, Dr. K. A. MacKenzie (chairman).

The annual meeting of 1937 will be held at Pictou.
ARTHUR L. MURPHY

Medical Societies

Brandon and District Medical Society and The Northwest Medical Society

A meeting of the Northwest Medical Society and the Brandon and District Medical Society was held at Clear Lake on September 9th, with a large attendance of doctors and their wives, 110 being present at the dinner. Dr. Geo. Clingan, Virden, President of the Manitoba Medical Association, presided. The chief subject of discussion was "Anterior poliomyelitis", and Dr. F. V. Bird, of Boissevain, where the present outbreak began, spoke of the clinical features of the disease and stressed the importance of administering convalescent serum as soon as possible, without waiting for too-well developed symptoms. Dr. C. R. Donovan dealt with the epidemiology. He considered that the protective properties of the nasopharyngeal mucous membranes could be enhanced with a spray of picric acid and sodium alum solution. Dr. N. R. Rawson lauded the value of convalescent serum; and Dr. E. L. Ross, of Ninette Sanatorium, mentioned the value of the respirator in tiding over a patient who had developed respiratory paralysis.

There was also a symposium on "Undulant fever", the speakers being Dr. J. N. Andrew, Minnedosa, Dr. C. R. Donovan, Department of Health, and Dr. N. R. Rawson, Brandon. Dr. G. S. Fahrni, Winnipeg, gave an address on "Upper abdominal pain". At the banquet, held in the main dining room of the chalet, Dr. S. J. S. Peirce, Brandon, spoke on the subject, "The doctor looks at politics". Mrs. George Clingan and Mrs. S. J. S. Peirce acted as hostesses.
ROSS MITCHELL

The Canadian Physiological Society

The Canadian Physiological Society, organized in Toronto in October, 1935, will hold its next meeting at Queen's University in Kingston, October 24th. There will be two scientific sessions, one in the afternoon, and one in the evening. The Society has now a membership of more than 160, and includes scientists from Prince Rupert to Halifax.

The Edmonton Academy of Medicine

During the past summer months, when regular meetings of the Academy are discontinued, the medical profession of Edmonton and vicinity have been especially favoured by having as visitors to our city several prominent members of the staffs of McGill and Toronto University Medical Faculties. During their short sojourn in the capital of Alberta the following meetings and clinics were arranged to which these distinguished visitors from the East generously contributed highly scientific and helpful addresses on the latest developments in medicine and surgery.

On June 17th, at a special meeting at which 110 members and guests were present, Dr. Duncan Graham, Professor of Medicine at Toronto University, read a paper on "Some problems in the diagnosis and treatment of peripheral arterial disease". He dealt with various aspects of peripheral vascular disease, including arteriosclerosis, thrombo-angiitis obliterans and Raynaud's disease. The paper was discussed by Drs. Pope and Hurlburt. Dr. F. F. Tisdall, Associate Professor of Pædiatrics, University of Toronto, also contributed a paper, illustrated by a series of lantern slides, in which he outlined much original, interesting work in nutrition and discussed its clinical application. The paper was discussed by Dr. Leitch.

On July 6th, at a special meeting of the Academy held at the University Hospital, Dr. F. S. Patch gave a bedside clinic at which the following cases were presented: (1) Ruptured urethra; (2) pyonephrosis; (3) tumour of the kidney in a child. Dr. Patch, in an admirable fashion discussed the clinical diagnosis and treatment of these conditions. Following a luncheon, Dr. Patch, the guest speaker, gave an address on "Newer aspects of urology," in which he discussed the following subjects. The speaker outlined the value of trans-urethral resection of the prostate in selected cases and pointed out that it would not completely replace a suprapubic operation. The value of the use of uroselectan in visualizing the kidney pelvis was outlined. The speaker also discussed the newer urinary antiseptics and stated that these agents had a very limited application. He stressed the point that the physician should try to determine the causative factors in urinary infections and remove them. The meeting was

well attended, a number of physicians from outside the city being also present.

On July 9th a largely attended meeting of the Academy took place at the Royal Alexandra Hospital to hear Dr. Roscoe Graham. Dr. Gordon Gray, president, was in the chair. Dr. Graham gave a very interesting clinic on a number of cases, covering various problems of surgical diagnosis and treatment. The speaker's methods of presenting these cases was very much appreciated. Through the courtesy of Dr. Anderson, Medical Superintendent of the Hospital, lunch was served, after which Dr. Graham again addressed the Academy on "Safety factors in abdominal surgery". Dr. Graham's visit was very much enjoyed and he well sustained his reputation as one of the outstanding teachers and clinicians in America.

T. H. WHITELAW.

The Peace River District Medical Association

The Annual Meeting of the Peace River District Association was held at Dunvegan on August 12th, 1936, when the following visitors were present: Dr. Fulton Gillespie, of Edmonton, President-Elect of the Alberta Division, the Canadian Medical Association; Dr. F. J. Folinsbee, of Edmonton; Mr. W. G. Hunt, Calgary, Associate Secretary, the Alberta Division, the Canadian Medical Association.

A discussion of the question of organized medicine in Canada was led by Dr. Gillespie.

The meeting recommended to the consideration of the Council of the College of Physicians and Surgeons, that a new electoral constituency for the Council be established for the Peace River District. The old officers were re-elected.

Following the discussion Dr. Gillespie read a paper on "Rectal ailments" and Dr. Folinsbee one on "Infant feeding and the deficient child".

A scientific meeting was held on August the 11th at Peace River. Among the members present were Dr. Percy Jackson, from Keg River, about 200 miles north of steel. At this meeting Drs. Gillespie and Folinsbee gave papers.

Camrose District Meeting was held at Camrose in August, the following provincial officers being present: Dr. D. S. Macnab, Calgary, President of the Alberta Division, Canadian Medical Association; also Dr. I. R. Bell, Coronation, who gave a scientific paper.

It seems an inseparable accompaniment of the advancement of knowledge that things once thought to be units turn out to be composites: the magic prism of investigation is always splitting up apparent entities into an ever-increasing number of new elements.—E. O. Jordan, *J. Prev. Med.*, 1929, 3: 279.

Post-Graduate Courses

The Montreal Medico-Chirurgical Society

The Montreal Medico-Chirurgical Society will hold its Fourth Annual Clinical Convention in conjunction with the Reunion of Graduates of McGill University, on October 21 to 24, 1936.

Interesting and varied clinical sessions are being planned by the Program Committee. These sessions will be held in the Royal Victoria Hospital, the Montreal General Hospital, the Royal Victoria Montreal Maternity Hospital, the Children's Memorial Hospital, and McGill University, and will run continuously on the above dates as follows:—

Wednesday, October 21st.—All day. Montreal General Hospital.

Thursday, October 22nd.—Morning. Children's Memorial Hospital.

Friday, October 23rd.—All day. Royal Victoria Hospital.

Saturday, October 24th.—Morning. Royal Victoria Montreal Maternity Hospital.

University Notes

Dalhousie University

The Dalhousie Medical School resumed classes with what will probably prove to be the largest enrolment in its history. First year registration stands at 60, of whom 50 are from the Maritime provinces. The primary purpose of a university is the education of its own people and so large a local representation is gratifying to the faculty.

Newly appointed to the chair of Physiology is Dr. Charles B. Weld, a 1929 graduate in medicine of Toronto University. Dr. Weld took his Arts degree at the University of British Columbia, where he also became a Master of Arts in bacteriology. Since 1922 he has spent much time in research, both in bacteriology and physiology. During the summers of 1926 and 1927 he was attached to the Marine Biology Station at Halifax. He interned at the Toronto General in 1929-30 and has been a Research Associate at Toronto University since, while carrying on a general practice in the city. In 1935-36 he was Assistant Professor of Physiology. His brilliant scholastic record, tempered by his years as a general practitioner, fits him well for his new position.

ARTHUR L. MURPHY

Special Correspondence

The London Letter

(From our own correspondent)

When all the institutions administered under the old "Poor Law" were transferred to the municipal and county council health authorities some years ago one of the stipulations, of a more or less permissive nature, was to the effect that close cooperation between the voluntary hospitals should be a matter of policy. So far this has not by any means been universally carried out, although in some cities (e.g., Manchester) a definite joint hospital policy has been formulated. Recently an accident case in Kent, many miles from London, was actually transported to Guy's Hospital because all the local voluntary hospitals were full and yet as subsequently transpired the local county hospital, near to the scene of the accident, could easily have admitted the injured patient. It has been estimated that the larger teaching hospitals in Great Britain have a waiting list which averages about 1,000 patients per institution and such patients could probably be accommodated without much difficulty if the municipal hospitals were properly used. It cannot be economically sound to keep working men and women waiting for cure of such conditions as hernia, and the modern accident problem tends to flood the teaching hospitals with emergency cases which might well go elsewhere. A special Voluntary Hospitals Commission is at present in session to try and secure some common policy, but what appears to be wanted is a wider survey of the whole hospital field, in order that the total beds available in whatever institution can be best rendered available for those who require them.

Last month Sir Herbert Barker demonstrated his manipulative methods before a special meeting of the British Orthopædic Association. This simple statement contains much of historic interest, for it recalls the controversies of past years when the famous bone-setter was the object of much popular sympathy, some of it as much misplaced as it was foolish. At the demonstration various patients received the special forms of treatment which Sir Herbert has himself devised. It is of interest that some of these are frankly empirical, and also that the president emphasized that all the orthopædic surgeons present now practise manipulation. Among the new appointments to His Majesty, King Edward VIII announced recently was the new one of "manipulative surgeon" filled, it may be stated with pride, by a medical man.

Medical care in industry has made great strides in the past few years, and the newly formed Association of Industrial Medical Officers now holds four meetings a year of medical men and women who devote the whole of their time to the subject of industrial medicine and hygiene. The September number of *The Practitioner* is devoted

largely to the subject of industrial medicine, suitably introduced by Sir John Simon, the present Home Secretary, who compares the position in industry now with what it was when he held his office twenty years ago. The importance of poisons, of lung disease, of psychological ailments, of skin disorders, and of absenteeism are some of the subjects dealt with by appropriate authorities, while the question of general hygiene and preventive measures receives adequate mention. In this connection the work of the Industrial Health Research Board is of great importance, and a recent report has dealt with conditions of comfort in factories. One of the findings was to the effect that cold air at foot level produces more discomfort than on the other parts of the body. The most comfortable temperature was about 65° F. but "comfort" was found to be experienced under a wide range of conditions. It is stated that part of future experiments planned on this subject is to include a study of the ventilation of the House of Lords, where, presumably, cold feet and hot heads may adversely affect the legislation of the nation!

Outside detective novels the highly trained medical investigator of crime does not exist in this country. There is no standard method of training those who conduct pathological investigations for the police, and indeed the whole subject of forensic medicine is rather the Cinderella of the medical curriculum. The newly-formed Metropolitan Police Laboratory offers certain facilities on a comparatively narrow basis. The Advisory Committee on the Scientific Investigation of Crime recommends unanimously something much wider—an institute with a recognized place in the academic sphere as a school of the University of London in the Faculty of Medicine. A certificate or diploma would be granted after a course of varying length, and on the pathological side there would soon be available a list of men suitable for selection by coroners for the performance of autopsies.

ALAN MONCRIEFF.

121 Harley St.,
London, W.C.1.

The Edinburgh Letter

(From our own correspondent)

The Annual Meeting of the British Medical Association held at Oxford under the presidency of Sir Farquhar Buzzard was an outstanding success. The environment further added distinction to the proceedings. The Association has expressed its warm thanks to the Local General Secretary, Dr. F. G. Hobson and his colleague, Dr. H. D. Woodroffe, to the Science Secretary, Dr. A. M. Cooke, and to the Chairman of the Executive Committee, Dr. W. Stobie. It has also expressed its indebtedness to the Vice-Chancellor of the University, to Mrs. Townsend, the Mayor, to Lord Nuffield and to many other persons who gave ungrudgingly of

their time and energy. The representative Meeting was presided over by Mr. H. S. Sellar and the elder statesmen in the persons of Dr. E. Kaye Le Fleming the Chairman of Council, Sir Henry Braletbury and Dr. C. O. Ravthorne, did much to enhance the interest and usefulness of the proceedings. That these proceedings were less controversial than usual is a tribute to the efficient work done by the Council during the year. Dr. W. Paterson, Chairman of the Dominions Committee, in giving approval of the section of the Report dealing with the Oversea Branches said that the representatives would realize that on the work of the members of the Oversea Branches depended the health and happiness of a very large number of the inhabitants of the British Empire, and that a debt was owing to them which could hardly be paid, especially as many of them worked under very trying conditions. Dr. Paterson also expressed the wish of the whole meeting that the forthcoming visit of Dr. G. C. Anderson, the Medical Secretary of the Association, to India would be very pleasant and successful. The Canadian Medical Association was represented by Dr. H. S. Birkett and Dr. A. H. Gordon, both of Montreal, and Dr. R. D. Rudolf, of Toronto. The meeting received with very great pleasure the greetings and good wishes sent by the Canadian Medical Association.

Sir Godfrey Collins, Secretary of State for Scotland, has introduced in the House of Commons the Maternity Services (Scotland) Bill. The main purpose of the Bill is to improve the standard of home midwifery and to secure adequate nursing and medical services for maternity in Scotland. The Bill supplements the existing provisions and envisages a comprehensive maternity service. It places on local authorities a duty to make arrangements for the provision to women in their own homes of the services both of a certified midwife and of a medical practitioner. The scheme provides for (1) medical examination and treatment during pregnancy, (2) medical supervision during the lying-in period, (3) medical examination at least once after the expiry of one month after child-birth, and (4) the services of an obstetrician to advise and assist where necessary. This is in accordance with the recommendations made in the Report of the Committee on Scottish Health Services which stated that "the service should be based on the doctor and midwife in concert, supplemented by consultants and adequate institutional facilities". The principle underlying the Bill is one of which the medical profession generally will heartily approve. It is that supervision of the expectant and nursing mother should normally be part of the family doctor's work. It will also be welcomed by midwives whose status and conditions of work in the past have been far from satisfactory. It is also probable that the reaction of the local authorities to the Bill will

be favourable, since the Bill realizes that different methods may be required in different areas especially with regard to such factors as difficulties of communication and sparseness of population. Further, new Exchequer grants to local authorities will be provided for the service. Provision is also made for preventing unqualified persons from practising as nurses in maternity cases, and for the attendance of midwives at courses of instruction. It is of interest to note that a Midwives Bill has recently been laid before the House of Commons with the object of improving the maternity service in England and Wales. This Bill is much more limited in scope than is the Scottish Bill. At the recent Annual Representative Meeting Sir Henry Braekenbury criticized the provisions of the Bill. He stated that it might be easier for a local authority, having set up a whole-time body of midwives, and having the power to appoint specialists, to use these midwives and specialists for the whole of the maternity work of the locality and exclude the general practitioner altogether. He proceeded to say that the public had been misled, with the best of motives and in complete good faith, by a number of eminent persons on this matter. The public had been led to believe that the maternal mortality of the country was very high and was a disgrace to the nation, whereas, if they compared statistics they would find that maternal mortality in England and Wales was among the lowest of the countries of the world. The public, he added, had also been led to believe that with extra care maternal mortality could be reduced by one-half. That statement required so many explanations and so many qualifications that stated in that crude way it was not true, or else it was meaningless.

R. W. CRAIG.

7 Drumsheugh Gardens,
Edinburgh.

Letters, Notes and Queries

Obstetrics in Equatorial Africa

To the Editor:

Dr. Rabinowitch's account of the Canadian Eskimos was extremely interesting. Practising among a Bantu people of equatorial Africa, I found his account of the birth of a child doubly interesting and a comparison of the two primitive methods may be instructive.

The dating of the obstetrical use of the bed-sheet to the Stone Age may be questioned from observations here. Many of the huts here are

built among boulders. Every hut has stones around the fireplace to which the sheets may be tied and plenty of posts to which a tie could be made. But I have never seen or heard of the use of any kind of "pullers". A banana-fibre rope would be thought of in primitive days when all births—as many now—took place in the banana shambe next to each hut. The use of chain "pullers" (made of auto mud chains) in the native hospital was not very popular among the patients nor among the native attendants. The patients much prefer to flex their knees and pull against their own ankles.

The primitive native birth customs here are not very physiological. When labour sets in the woman keeps the information to herself as long as possible, probably to obviate attention from the inevitable mass of villagers who attend the affair. The custom of the old women is to encourage pains and not to let the woman rest between pains. Even in the first stage the woman is encouraged and forced to bear down by beating, holding hands over the nose and mouth, etc. The result frequently is that the patient is tired out before the second stage is passed and those pains are weakened. Then an injection of pituitrin or terminal forceps is extremely useful after she is brought to the hospital.

When left to herself with severe pains the woman will crawl around the banana shambe on her all fours with her pendulous abdomen hanging half a foot below the outlet. The same stunt will take place in the delivery room if she is unwatched.

As with the Eskimos the actual birth takes place in a squatting position. An attendant sits behind the patient and grasps her arms around the patient below the latter's arms and squeezes hard over the fundus. Another attendant squats in front between the patient's legs, and throws cold water over the vulva or plasters it with cow dung, etc., if the labour is too prolonged. The cord is tied with a banana fibre and cut with it or a blade of grass. The baby is dashed over with cold water and laid aside uncovered even if the weather is damp or cool. No attempt is ever made to deliver the placenta. The cord is never pulled on nor the abdomen squeezed. This is inconvenient, as many times we are called for adherent placentas when they would fall out if the woman had merely stood up!

R. B. MICHENER

P.S.—Boys average 7 lbs. and the girls 6¾ lbs. Friends Hospital, Kaimosi, P.O. Kisumu, Kenya, East Africa. August 3, 1936.

Australasian Medical Congress

To the Editor:

Our Executive has instructed us to bring to your notice that the Fifth Session of the Australasian Medical Congress will be held at Adelaide, South Australia, from the 23rd to the 28th of August, 1937. Sir Henry Newland, Adelaide, has been nominated as President.

We have extended an invitation to your President, and also wish to invite any members of your Association who may be visiting Australia to become members of our Congress.

(Signed) ALLAN D. LAMPHIL,

C. B. SANGSTER,

Hon. Joint Secretaries.

Adelaide, South Australia.

March 19, 1936.

Hyperhidrosis

To the Editor:

How am I to clear up drenching perspiration of a woman of 49 in the menopause? Basal metabolic rate is -25. This woman is well nourished and active. Perspiration will actually soak her dress while you watch. "Pituvarium" of no use. Thyroid extract previously tried elsewhere increases the perspiration.

E. C. H. WINDELER

Windsor, Ontario.

August 1, 1936.

Will some of our readers give suggestions?

[Ed.]

Topics of Current Interest

BCG as a Tuberculosis Preventive

There are a number of reasons why the use of the living vaccine known as BCG, twelve years after its first use in France, should still be discussed and debated among those concerned with the prevention and cure of tuberculosis. It has never been conclusively demonstrated that the use of this vaccine is an effective means of preventing human tuberculosis. The reports of studies of its value as an effective vaccine in animals are greatly at variance despite the fact that these studies have been made by excellent investigators. The greatest value of BCG is in cattle but, in view of the variation in reported results, one could scarcely conclude that it is justifiable to use it universally in man. Those who have tried to produce a fixed virus without virulence, using a bile medium by the method of Calmette and Guérin, have failed to do so. Especially notable in this connection

are the studies of A. Stanley Griffith,¹ using seven bovine strains and exactly the method of the French scientists over a period of ten years. Yet he failed to alter the virus.

Since 1900 it has been well known that the injection of certain strains of tubercle bacilli raises the resistance of certain animals to a later killing dose of virulent tubercle bacilli. But the vaccination of man with living tubercle bacilli had never been seriously proposed until 1922, when Professor Calmette enthusiastically suggested it and French physicians began to practise it. This enthusiasm was not shared by British and American physicians, primarily because the determination as to whether it should be used in commerce was in Great Britain in the hands of the Medical Research Council and in the United States in the hands of the National Institute of Health (U. S. Public Health Service) and the Bureau of Animal Industry (Department of Agriculture), which are government agencies. Their conservatism was based on the premise that the ability of the vaccine to justify the claims of the French scientists should be proved by animal tests before employing it wholesale in man.

The enthusiasm with which the French scientists advocated their prophylactic vaccine received a severe blow from the American and British point of view when Prof. Major Greenwood² in England criticized the methods of statistical study that were used by Calmette to prove the value of his vaccine. There is still a great tendency to base conclusions on empirical observations rather than on rigid scientific technique in human epidemiologic studies, in which it is so difficult and so important to provide comparable controls.

The method of administering the vaccine has changed three times in this period. Administration by mouth in the early days of life was first advocated. This apparently is gradually disappearing as a method of election. The next method was administration by subcutaneous injection. This was so frequently followed by "cold abscesses" that this also is gradually giving place to the method of intracutaneous injection. Experiments in animals have shown little value for the oral method as a means of prevention. The subcutaneous method and the intracutaneous method are variable in their results in animals. The intravenous method³ of vaccination has proved to be the most efficacious in cattle, although this also varies within wide limits. The greatest difficulty has been to determine how long the period of increased resistance lasts. This also apparently varies in many instances and is often of short duration; that is, under one year.

Many different cultures of BCG have been

1. GRIFFITH, A. S.: *The Lancet*, 1932, 1: 303, 361.

2. GREENWOOD, MAJOR: *Brit. M. J.*, 1928, 1: 793.

3. BEXTON, J. B. AND GRIFFITH, A. S.: *The Lancet*, 1931, 1: 393.

sent to the United States in the hands of various persons, laymen and physicians alike. Different workers have used cultures obtained at different times from the French laboratories. The result is variation in the experimental work that has been carried on, for little has been done to check the constancy of the characteristics of these strains. When the matter of human use first required attention in the United States, Dr. G. W. McCoy, director of the National Institute of Health, conferred with Dr. Theobald Smith, Dr. William H. Park, Dr. Eugene L. Opie and Dr. William Charles White. It was agreed that Dr. Park and Dr. Opie should undertake to use the vaccine (with the consent of parents) in children in the United States with as careful control conditions as possible. These studies were undertaken with the approval of Dr. McCoy. One study⁴ was carried on from the Department of Health of New York City and the other⁵ from the Henry Phipps Institute in Philadelphia. The results of these studies have been published from time to time. They are among the best attempts in the world at adequate control comparisons, but one can only conclude, after studying them, that they do not provide conclusive evidence for general use of the vaccine.

It is not the purpose here to analyze the experiments by various persons in different countries but rather to offer certain conclusions based on a careful study of the data and a familiarity with several of the experiments in different countries. The whole subject has been fairly reviewed by K. Neville Irvine.⁶ It may be concluded that:

1. Practically all strains of BCG used in children have been avirulent. (Nothing has been said of the Lubeck disaster, as this was proved to be a laboratory accident.)

2. It has been proved that there is a definite increase in the resistance of cattle by the use of this vaccine, although it varies within wide limits and the duration of the increased resistance also varies within wide limits.

3. The evidence of increased resistance produced by this vaccine in many other species of animals is not very convincing.

4. The oral method, if one is to judge by animal experiments, is not efficient.

5. One is not justified in taking the animal experiments, even those in cattle, as a reason for universal vaccination in man.

Sufficient arguments can however be presented for the use of this vaccine in groups for which

little can be done by other methods, as for example the Negroes in the South and the Indians on the reservations, where the present machinery is not adequate in view of the peculiar circumstances surrounding their condition. It would be possible, under conditions in which a high death rate prevails, over a period of twenty years, to determine something of the value of BCG and also to add to our knowledge. That there is no conclusive proof of the efficacy of the vaccine in man is in part due to the short duration of the experiments and to the small number of those involved in the carefully controlled experiments as well as to the inadequacy of the accurate data on the control groups.—Editorial, *J. Am. M. Ass.*, 1936, 107: 132.

Studies in Colds and Influenza

Several bands of patient and privileged workers continue to wrestle with the problem of virus diseases of the respiratory tract. That such work emanates principally from two centres only is due to the fact that unlimited time and expensive facilities are needed for its successful prosecution. Interest has lately been centred on the achievement in this country of propagating the virus of influenza in ferrets and in mice. It need hardly be pointed out that the ability to produce a disease at will in an experimental animal, and to maintain individual strains of the causative micro-organism in this way, is an important step forward and opens the door to new methods of study. One of these is the demonstration of antibodies in human serum by means of protection tests in animals, and experiments on these lines now reported from the United States yield some interesting and puzzling results. Francis and Magill¹ have found that neutralizing antibodies for the virus of influenza are demonstrable in a large proportion of human sera; the puzzling feature of their results is that although the age period 30 to 39 furnishes the biggest percentage of sera containing antibody, the period in which this antibody is most often present in sufficient amount to give complete protection is from 1 to 5 years. Studies by Francis and Shope² suggest that there is some antigenic relation, by no means amounting to identity, between the viruses of human and swine influenza, and Shope³ in another paper, which describes the results of protection tests with human sera and the virus of swine influenza, suggests not for the first time that this virus is the "surviving prototype" of that responsible for the human pandemic of 1918. Meanwhile Dochez and his colleagues,⁴ in transmitting influenza virus to human volunteers, have produced more often

4. KERESZTURI, CAMILLE, PARK, W. H., VOGEL, P. AND LEVINE, M.: Fate of children of tuberculous families, including those treated and those not treated with BCG, *Am. J. Dis. Child.*, 1934, 48: 507.

5. ARONSON, J. D. AND DANNENBERG, A. M.: Effect of vaccination with BCG on tuberculosis in infancy and in childhood, *Am. J. Dis. Child.*, 1935, 50: 1117.

6. IRVINE, K. N.: *The BCG Vaccine*, Oxford University Press, London, Humphrey Milford, 1934.

1. *J. Exper. Med.*, 1936, 63: 655.

2. *Ibid.*, 1936, 63: 645.

3. *Ibid.*, 1936, 63: 669.

4. *Ibid.*, 1936, 63: 559, 581.

than not simply a common cold, a result which they are not prepared at present to explain. They have also maintained strains of common-cold virus in culture in a chick-embryo medium through eighty and more generations, and have reproduced the disease in volunteers by intranasal installation of these cultures. Dochez has found that the preservation *in vitro* of the cold virus is favoured by the addition of gum acacia. This paper records over one hundred such inoculations of human beings, and mentions that the victims were accommodated in private wards and nursed under the most stringent conditions (stopping short, however, of the actual sterilization of their food) to prevent extraneous infection; but we are not told who they were and by what means or at what expense they were induced to undergo this treatment. Obviously the resources necessary for experiments of this kind are a bar to their execution by all but a few investigators. In one direction only do these observations appear to bear directly on the ultimate aim of all this work—a method of prophylaxis. Necessary and illuminating as all these studies are, there is still one fact which seems to stand immovably in the way of their practical fruition, and that is the evanescence of the immunity conferred by the natural infection. Artificial immunization can scarcely hope to improve on this, and it is therefore difficult to see how such a method could be applied without a degree of trouble disproportionate to the value of its results.—*Brit. M. J.*, 1936, 2: 29.

Coramine as an Antidote to the Barbiturates

The great efficacy of coramine as a stimulant to respiration has been recognized for some years. It was recently discussed at a meeting of the section of therapeutics and pharmacology of the Royal Society of Medicine, where, though a little doubt was thrown on its value, the majority expressed their faith in the drug, and some described excellent results obtained from its use in all conditions associated with shock and depressed circulatory and respiratory states. Anaesthetists have often used injections of the drug to improve the breathing when it has shown signs of failing or has actually stopped. This action of coramine has been taken advantage of especially in connection with depression of respiration arising after the use of basal narcotics. An interesting series of clinical experiments is described by Dr. P. G. Schube, which shows the remarkable power possessed by coramine of counteracting the effects of barbiturates. It is not merely the increased depth and frequency of respiration and improved circulation which follow the administration of coramine, but also the extraordinary cutting-short of the unconsciousness that had been induced by large amounts of barbiturate. The

opportunity to test these results arose in the psychiatric clinic of the Boston State Hospital, the patients being all "mentally ill but physically normal". Tests were carried out on 84 patients, the controls receiving barbiturate but no coramine. In the other patients the coramine was given intravenously 5 c.cm. first, and if consciousness had not returned at the end of ten minutes another 5 c.cm. every ten minutes until the patient was conscious. It is stated that in each instance when coramine was injected "the state of unconsciousness was abolished, some persons having to receive more coramine than others to achieve this result". In the controls, unconsciousness lasted for hours longer than in those that had had coramine, in whom it was only a matter of minutes. It is notable that in all these patients the pulse-rate and volume were unaltered although respirations were increased both in rate and in depth. Some of the patients vomited after 10 c.cm. of coramine had been injected. There were no after-effects, and the author concludes that "coramine is an excellent drug to counteract effects produced by barbiturates".—From *The Lancet*, 1936, 1: 1420.

Medico-Legal

XXIII.

The Evidence of a Bullet Wound

Medico-legal evidence may be of overwhelming importance in proving or disproving guilt. But such evidence often calls for very careful observation. Both these points are well brought out in a case reported by Osborn (*The Lancet*, 1936, 230: 1295). The main point to be decided was whether the victim had been shot from behind or from in front. The accused admitted the shooting, but said that he had fired in self-defence, facing his man; to which the prosecution replied that the nature of the wound showed that it must have been inflicted from behind, making the presumption of wilful murder very strong.

The wound was in two parts; a large and ragged opening at the external angle of the right eye, and a small, clean hole behind this, immediately above the right ear. The brain substance on the right side was extensively macerated, and contained fragments of bone and two pellets of lead. From these findings the Crown examiner concluded that the small clean hole posteriorly was the entry wound, and the large ragged hole anteriorly the exit, from which it followed that the bullet must have been fired from behind. This decision was based on the

widespread belief that bullets make a small wound on entry and a large one on exit, but the defence pointed out that the nature of bullet wounds depends on (a) the kind of bullet, (b) the muzzle velocity of the weapon, and (c) the range at which the shot is fired. In this case, the bullet was of lead with no hard jacket. Such bullets act as dum-dums, immediately mushrooming out on striking the body, and so causing extensive tissue damage at the point of entrance, probably more than at the exit. Again, even if the bullet is hard, (i.e., nickel-jacketed) it is more apt to "wobble" when the muzzle velocity is not very high, and thus to lacerate the tissues at the point of entry. And, finally, at short range, any bullet is apt to cause a large entry wound, as its impact on the tissues is so terrific (virtually an explosion).

To account for the small clean hole, it was shown that the soft lead bullet had broken into three small pieces in smashing through the cranium bone, and that one of these pieces had followed the lateral wall of the skull till it reached the curve-in of the posterior region of the ear. Here it went through and dropped to the floor, where it was found later on.

Another point brought out was the absence of powder-marking around either wound. As the powder used was black and the distance from which the shot was fired very short, only about four feet, there must have been some powder deposited on the tissues at the point of entry, but there was no marking around the small posterior wound. On the other hand, the anterior wound was so extensive that the area of scalp receiving the powder mark had been blown away. There were other arguments, less striking perhaps, but all tending to prove the same thing, i.e., that the bullet must have been fired from in front of the victim, and, accordingly, a verdict of not guilty was finally brought in. Later on, additional suggestions were made by Sir Sydney Smith which brought out even more facts for consideration. He said that if the margin of the wounds in the bone had been examined closely, extremely important evidence could have been gathered by noting the angle of bevelling caused by the bullet. Almost invariably the bone bevels in the direction of fire, so that in this case the posterior wound would have shown at once whether the missile entered or left the skull at that point. Secondly, it was suggested that the fragments of bone found in the brain tissue might have been examined to see if they corresponded with the loss of bone at the posterior opening. If their total area was greater than the loss of bone at this opening, then they must have been driven in by the bullet entering at the anterior wound, for obviously if this were the exit wound, all bone fragments would have been blown outside the skull.

H.E.M.

Abstracts from Current Literature

Medicine

Artificial Pneumothorax in Lobar Pneumonia.

Blake, F. G., Howard, M. E. and Hull, W. S., *Medicine*, 1936, 15: 1.

This article begins with a useful historical summary and analysis of the subject up to date, and also of the various theories advanced as to the influence of artificial pneumothorax on the course of lobar pneumonia. The authors then give their observations and conclusions based on a study of 42 cases in the New Haven Hospital, New Haven, Conn. As a result of certain preliminary experiments they think that the view that lobar pneumonia is a bronchogenic infection, the inception of which is not dependent upon the occlusion of a bronchus by an infected mucous plug, is the most acceptable. Their subsequent observations support the theory that artificial pneumothorax in this disease exerts its influence by limiting or abolishing the constant expansile and contractile motion of the involved lung during respiration and not by accelerating the production of antibodies or by expelling bronchial exudate and draining the lung of inflammatory products. The "lung rest theory" of therapeutics by artificial pneumothorax is to them the most reasonable, even though no evidence has been developed as yet to show in what manner collapse and immobilization of the pneumonic lung, apart from relieving pleural pain, exert a beneficial influence. The induction of artificial pneumothorax is, they conclude, an emergency procedure, and should be carried out without delay early in the course of the disease if a really beneficial effect on the course and outcome of lobar pneumonia is to be obtained. The longer the procedure is delayed, the less likely are the results to be satisfactory. No statistical analysis of their results is warranted, but they think the procedure is worthy of further trial.

A. G. NICHOLS

The Psychology of the Tuberculous. Learoyd.

C. G., *Brit. J. Tuberc.*, 1936, 30: 111.

The author of this arresting paper asks "Is there an attitude of mind characteristic of the tuberculous? Does the toxin produce anything comparable to the relentless depression of influenza, the abject apathy of ankylostomiasis, or the cunning mendacity of opium? It is at once to suppose that a disease that can modify the rest of the body, so as to give rise, for instance, to the 'tuberculous facies', would not at the same time modify the mental processes. Young patients, especially those with glandular and bone tuberculosis, tend to have mental characteristics of their own; they are gentle and kindly, enthusiastic and excitable, imaginative and amenable, and as a rule content. In the case of

pulmonary tuberculosis, when the action of the toxin is intermittent, the mental state varies, corresponding with the periodic activity of the disease. Anyone who has had a temperature from tuberculosis will recognize that "Treasure Island" faithfully reproduces the tempo of his thoughts. Fishberg has given a long list of authors and poets in whom the toxin of tuberculosis, we may suppose, has supplied some at least of the stimulus to their creative mental processes. Probably the best thing for a tuberculous writer is to be a "leaker", that is, one in whom small quantities of toxin are liberated from time to time, but never in sufficient amounts to do harm. Learoyd thinks that one characteristic of the tuberculous at all times is that their normal attributes, especially, perhaps, their expansive ones, are accentuated—the adventurous becomes more adventurous, the cheery more cheery, and the generous more generous. One very marked type of mentality is not nearly so common in these days of controlled temperature as it used to be—the fervid, fiery, febrile type, the extrovert with a mission and the tuberculous toxin as a driving force within him—a type that is also met with in the alcoholic. There are some who regard a certain cantankerousness, a desire to hurt, a "wasppishness", as part of the abnormal mental state of the tuberculous subject. Surely, this is but a normal reaction to adverse circumstances. The young man with his career shattered, the brand of Naaman imagined, cribbed, cabined and confined, or the married man with the clouds of financial embarrassment threatening him, is merely reacting normally to hard conditions. Who would not be the same under similar provocation?

A. G. NICHOLLS

Surgery

Relation of Pathological Changes of the Intervertebral Discs to Pain in the Lower Part of the Back. Sashin, D., *Arch. Surg.*, 1936, 32: 932.

In this article, Sashin draws attention to the importance of pathological changes of the intervertebral discs, particularly those of the lower portion of the spine and of the lumbosacral junction, in the causation of pain in the lower part of the back.

The discs form one-quarter of the total length of the spine. They vary in size, being widest and thickest in the lumbar region and smallest in the dorsal region. In the lumbar region they form a third of its length. They have no blood vessels, but receive nourishment from the bone marrow of the bodies by diffusion. These discs permit a considerable range of motion and impart great flexibility to the spine. They act as a buffer or shock absorber for the strain and stress of daily activity. Mobility of the spine is

greatest in the cervical and lumbar regions and least in the dorsal. Flexion is freest and most extensive in the lower lumbar portion of the spine. Pathological changes in the intervertebral discs are mainly seen after the third decade of life and increase in frequency with age. The changes vary from a small herniation from the disc into the vertebral bodies, to beginning vascular infiltration of the substance of the disc, fibrous replacement of nuclear tissue, brown degeneration, calcification of the nucleus and in later stages, shrinkage, narrowing, and ossification of the disc. The flexibility and mobility of the spine are considerably diminished when degenerative changes are present. Herniation from the discs into the adjacent bodies is frequently found post mortem. These invasions are usually of small size, but, often may extend for a considerable distance into the substantia spongiosa. The great majority of herniations are not visualized by x-rays. Marked degenerative changes of the substances of the disc are often seen, without any evidence of herniation. These changes result from the wear and tear of daily activity. The clinical picture of pathological discs is not clearly demonstrable. The main symptoms complained of are dull aching pains in the lower part of the back, pain radiating down the backs of the lower limbs along the course of the sciatic nerve. There is frequently the history of a slight injury, a slight fall or a sudden twist on lifting an object. The lower lumbar portion of the spine is held rigid; motion of the spine is restricted. There is tenderness over the lumbosacral junction as well as over the area supplied by the superior gluteal nerve. The author's treatment consisted in an attempt to re-establish the normal lumbar lordosis and to support the spine by means of a plaster of Paris jacket. He obtained the best results by gently hyperextending the spine while the patient was under general anaesthesia, until the normal lumbar lordosis was reached, then applying a plaster of Paris jacket from the upper part of the chest to the pelvis.

G. E. LEARMONTH

Obstetrics and Gynæcology

Regional Anæsthesia in the Conduct of Labour.

Walker, A. T., *Am. J. Obst. & Gyn.* 1936, 32: 60.

Local block and infiltration anaesthesia have a wide application in obstetrics in the conduct of labour. Most labours can be conducted and successfully terminated with a minimum of pain, low morbidity and mortality by the use of the type of anaesthesia and analgesia described. Many patients so handled do not remember the labour or the delivery.

Abnormal presentations and labours can be successfully conducted with this type of anaesthesia. Episiotomy and repair can be accom-

plished with the same anæsthesia as used for the delivery. Although no definite statistics are available at present, the blood loss during and after the third stage appears to be much reduced with regional anæsthesia.

In addition to producing a relatively painless labour and delivery regional anæsthesia demands careful handling of instruments and respect for tissues which ultimately reduce morbidity and mortality in both mother and infant, and, therefore, constitutes one of the major advantages of this method.

ROSS MITCHELL

A Study of Three Hundred and Eight Cases of Placenta Prævia. Irving, F. C., *Am. J. Obst. & Gyn.*, 1936, 32: 36.

A study of 308 consecutive cases of placenta prævia at the Boston Lying-In Hospital shows a decrease in maternal mortality from 11.6 per cent to 2 per cent, and a decrease in net fetal mortality from 47 to 20.3 per cent. In clean cases, where the infant is alive, normal, and of an estimated weight over 4 pounds, Cæsarean section offers about an 85 per cent chance of securing a living child, with a risk to the mother not exceeding 5 per cent.

In clean cases, when the infant is dead, deformed, or under 4 pounds in estimated weight, Braxton Hicks version may be performed by the trained obstetrician at no greater risk to the mother than Cæsarean section. In clean cases of marginal placenta prævia, simple rupture of the membranes deserves an extended trial. It is safe for the mother, and apparently less injurious to the child than has been supposed. In infected cases, Cæsarean section followed by hysterectomy is the operation of choice, regardless of the condition of the child.

ROSS MITCHELL

Pædiatrics

Prognosis of Rheumatic Infection in Childhood.

Ash, R., *Am. J. Dis. Child.*, 1936, 52: 28.

This is a study of 445 children coming under observation for rheumatic fever at the Children's Hospital, Philadelphia, during the period 1922 to 1932. Ninety-three per cent of these children were observed for an average period of seven and a half years after the onset of their disease. At the end of this time 66 per cent showed valvular disease of the heart and 22 per cent had died.

The course of the affection was modified by such variables as race, sex, age and the calendar year of the origin.

Among the clinical manifestations which were of the most serious omen were pericarditis, rheumatic pneumonia, involvement of both mitral and aortic valves, the early appearance of a button-hole mitral stenosis, and obtrusively

large subcutaneous nodules. Chorea, in itself, was a mild manifestation. In an intermediate group may be placed epistaxis, abdominal pain, hæmaturia, and the multiform cutaneous eruptions.

The crucial period for treatment is during the first year after the inception of the disease, inasmuch as when permanent cardiac damage occurs it does so before the end of the second year after the onset.

JOHN NICHOLLS

Appendicular Symptoms in the Acute Infectious Diseases. Ronaldson, G. W., *Brit. J. Dis. Child.*, 1936, 33: 85.

The appendix is frequently involved in the acute infectious diseases, though suppurative appendicitis is rare. Appendicitis is mentioned as a complication of scarlet fever, measles, small-pox, rubella, typhoid and malaria. Some French authors attach considerable importance to its supposed relationship to scarlet fever.

Ronaldson finds that in London appendicitis severe enough to call for operation in cases of infectious disease is quite rare. In one London infectious hospital, in 20,000 cases, there were only 2 operations for appendicectomy; in another there was only 1 appendicectomy (in scarlet fever) in a series of 7,659 fever cases. He reports two cases of his own of operation for acute appendicitis, one with abscess and one with gangrene, in scarlet fever, at the South-eastern Hospital. These cases are illustrations of the well-recognized fact that abdominal conditions in young subjects may pursue an insidious course and so occasion difficulty in diagnosis. In these cases the association of appendicitis with scarlet fever may have been quite fortuitous. He states further, that though suppurative appendicitis is very rare in measles pain localized to the iliac region may be an early feature in that disease. These are the cases of what Mayerhofer calls "pseudo-appendicitis". It is important to remember that this symptom may occasionally be present. When the eruption of measles occurs on the fourth day, the tendency is for the acute iliac pain to subside. The discovery of Koplik spots will establish the diagnosis and prevent the hasty surgical interference.

JOHN NICHOLLS

Morquio's Disease. Report of Two Cases. Summerfeldt, P. and Brown, A., *Arch. Dis. Childhood*, 1936, 11: 221.

This rare condition, of which only 18 cases have been reported in the literature according to the authors, is characterized by dwarfism, deformity of the body due to changes occurring chiefly in the vertebrae, pelvis and long bones caused by delayed epiphyseal development and retarded ossification. Only 3 of the 18 have been isolated cases: the remaining 15 have occurred

in children where other members of the family were affected. The family reported by the authors consisted of two normal girls, two normal boys, and two affected boys. The parents were not related. The use of pituitary and thyroid extract and of viosterol by other authors proved of no benefit. The younger of the children in this family was put on cod liver oil and calcium tablets, the latter only being taken. The mother reported that he had gained in height, an observation not yet confirmed by examination by the physician. The older boy was given thyroid. No statement as to the result was given.

MADGE THURLOW MACKLIN

Pathology and Experimental Medicine

The Moppet Test for Cancer. Welsh, D. A., *J. Cancer Res. Com. Univ. of Sydney*, 1936, 7: 132.

Professor Welsh gives a review of the Moppet test with valuable comments. Briefly, the test is as follows. The blood to be tested and blood from a healthy control are placed in opposite ends of a special diffusion vessel which is filled with normal saline after the bloods have clotted. A fragment of mouse tumour (sarcoma) is placed on a glass plate, which is then inverted over the diffusion vessel so that the fragment of tumour lies midway between the two clots. An initial reading (drawing) is taken of the periphery of the tumour fragment. The diffusion vessel is then incubated at 37° C. and the readings are taken at one hour and at twenty-four hours. In a negative reaction there is a more or less symmetrical "outwandering" of cells from the fragment of sarcoma; in a positive test for cancer there is a definite "sweeping" movement of the sarcoma cells away from the cancerous patient's blood.

Dr. Moppet has given the results of 23 tests made on unknown bloods in addition to those of the 30 published in an earlier paper. Of the 23 tests 8 gave a positive reaction for cancer, and of these eight 5 were correct and 3 were incorrect. Admittedly, this is a poor showing and indicates the necessity for further improvement in the technique. However, both in its successes and its failures the test has raised questions of great scientific interest and promises to be of practical value.

Dr. E. F. Thomson has, also, made an independent investigation of the test, covering 100 cases, with unexpectedly good results. Thirty-six gave a positive reaction for cancer, 33 of which were in patients clinically cancerous and 3 in patients not clinically cancerous. According to the available evidence, however, these 3 had probably developed cancer at some time. It is noteworthy that the 33 positive reactions were found in patients in the early stages of cancer,

before anaemia and wasting had occurred. Objection might be taken that these 33 correct positive findings for cancer were of little practical value, inasmuch as a biopsy might have been made in all or nearly all of the cases, but this is not the point. The significant fact is that a correct positive cancer reaction was found in 92 per cent of cancers in the early stages from many different anatomical sites. This suggests that the Moppet test has a scientific significance which must be farther explored before its clinical usefulness can be properly assessed.

JOHN NICHOLLS

Amidopyrine and the Circulating Leucocytes.

Simon, S. D. and Metz, M. H., *J. Lab. & Clin. Med.*, 1936, 21: 1154.

There is little doubt that in certain persons amidopyrine is competent to produce granulocytopenia; there is no doubt in most minds that the vast majority of people can take the drug without developing this condition. This latter statement would seem to be self-evident and yet it rests on no proper basis of investigation. The authors, therefore, have endeavoured to supply the lacking evidence. Their paper is based on the study of 103 patients whose history was followed up for an adequate length of time. Those suffering from severe disease of the heart or the blood-forming organs were excluded from the test. The majority of the persons studied were in the 5th, 6th and 7th decades of life; the remainder were scattered fairly uniformly in the 2nd, 3rd, 4th and 8th. All received amidopyrine, and 20 of them in addition received isoamylethyl barbituric acid (amytal). In not a single instance did a significant decrease in the number of leucocytes occur. In one case an actual leucocytosis was observed (the highest count was 16,000 with 86 per cent neutrophils), accompanied by nausea and malaise. The total amount of amidopyrine given varied in the different cases from 14 to 49 grams, spread over 14 to 49 days. The sedimentation rate was not affected in any of the 8 cases in which this test was performed. No morphological alterations, such as "toxic granules" in the neutrophils, were observed. The differential count, also, was not affected in any significant fashion.

The authors conclude that the entirely negative results of their experiment would seem to substantiate the widely-held opinion that granulocytopenia when associated with amidopyrine medication is a matter of individual susceptibility.

JOHN NICHOLLS

Morphological Changes in the Heart in Experimental Myxœdema.

Webster, B. and Cooke, C., *Arch. Int. Med.*, 1936, 58: 269.

The question is raised as to whether in myxœdema cardiac enlargement and the presence

of low voltage in electrocardiograms are found. The authors have investigated the problem by removing the thyroids from a group of rabbits and examining the hearts after a considerable lapse of time. Their autopsy findings were compared with similar tissues from controls.

There was some variation in the degree, but myxœdema was produced in all cases, corroborated by an increased blood-cholesterol content, loss of hair, and in some cases effusions into the serous cavities. The hearts of all thyroidectomized animals were pale and flabby, with increased fluid content. The muscle stained poorly, the fibres were swollen, with loss of fibres, especially of the transverse type. The nuclei stained deeply and were surrounded by a clear area, not composed of fat. The aortas showed very little change. Some atrophy of testicular and ovarian tissue was noted. Electrocardiograms showed a gradually decreasing voltage, as registered by the height of the T-wave and the Q.R.S. complex.

P. M. MACDONNELL

Therapeutics

The Treatment of Carcinoma of Cervix Uteri by the Stockholm Technique at the London Hospital. Brews, A., *The Lancet*, 1936, 1: 713.

In two years, 1929 and 1930, seventy-one cases of cancer of cervix were treated at the London Hospital. Of these, four selected had Wertheim's hysterectomy done, with the subsequent history that one died of recurrence one year and five months after operation; one died of recurrence two years and eight months after operation; one, last seen one year and nine months after operation, was alive and well; and one is alive and well more than five years after operation. The remaining 67 cases were treated by radium, by the Forssell-Heyman technique from Radiumhemmet, Stockholm, e.g., 120 mg. of radium, three applications at seven and twenty-one day intervals; duration of each application 22 to 24 hours; screenage 2 mm. of lead in 1929 and 3 mm. of lead in 1930; partly intra-uterine and partly vaginal. No case, however advanced, was refused treatment.

The diagnosis was confirmed in all but 8 cases by histological examination.

The results show 16 five-year cures out of 67 treated by radium, or 24 per cent. On grouping the 67 cases into the four stages according to the anatomical extent of the growth, as recommended by the Radiological Sub-Commission of the League of Nations, Geneva, 1929, the first stage showed 40 per cent five-year cures; the second, 30 per cent; the third, 16.6 per cent; the fourth, none. The first and second stages are probably operable, and if the results are combined they show 34.3 per cent five-year cures.

The third and fourth stages are probably unoperable and combined show 12.5 per cent five-year cures. At Radiumhemmet, Stockholm, in ten years, from 1920 to 1929, they treated 1,295 cases of carcinoma of the cervix, with 23.8 per cent five-year cures.

S. A. McFETRIDGE

The Effect of Oophorectomy and Splenectomy on Cancer of the Breast and Uterus. Paterson, P., *The Lancet*, 1936, 1: 1402.

The unlimited multiplication of the cells in cancer is generally explained by two factors—first, the abnormal stimulation of the cells primarily involved; and second, the medium in which these can grow. The author considers the latter the more important. He offers no opinion as to the cause of this change which takes place in the tissues. He gives examples of tumours which were proved to be malignant and have disappeared spontaneously. The first case was a young woman who, one year following appendectomy, developed a mass in the right iliac fossa. At operation, the mass involved the cæcum. Microscopically, it was shown to be a spindle-celled sarcoma. Following operation, a large abscess developed (*B. coli*), and when this cleared up the mass gradually disappeared and today she is alive and well.

The second case was carcinoma of the stomach, with secondaries in the liver. This was confirmed by microscopic examination. Nothing further surgical was done, except to close the abdomen, and the patient is alive and apparently well today.

The high immunity of the spleen to primary and secondary cancer suggested trying to use an extract to control cancer. As a result of these injections, Paterson came to the conclusion that the growth was stimulated by these injections, and the larger the dose, the more rapidly did it advance. Consequently, he tried removal of the spleen.

The third case was a woman of 41 years of age, who two years previously had had both ovaries and uterus removed for adeno-carcinoma of the uterus. She now had a secondary tumour in her pelvis, involving the rectum (blood pus and mucus) and bladder (urine containing pus and blood). She required narcotics for pain and sleep. A left inguinal colostomy and splenectomy were done, followed by 4 c.cm. daily of splenic extract for six weeks. Her condition became progressively worse, but improved when 1 c.cm. was given daily for two months. Now, four years later, there is no evidence of disease.

The fourth case was a woman, 46 years of age, with cancer of the right breast of at least one year's duration. The mass was firmly fixed to the chest wall, there were glands in axilla, skin nodules and widespread lymphatic involvement. Microscopic examination of the glands showed

adenocarcinoma. The spleen and both ovaries were removed. No other treatment was given. Ten months after operation the lymph glands in the axilla were no longer palpable, the entaneous nodules had all disappeared, and the breast was a shrivelled fibrous mass. The patient gained a stone in weight.

Removal of the ovaries or the spleen does not affect the course of the cancer, and these cases were just presented as a possible help or guide to other workers in this field.

S. A. McFETRIDGE

The Treatment of Surgical Infections with the New Chlorine Solutions. Young F., *Surg., Gyn. & Obst.*, 1936, 63: 318.

The author reports on the use of a new chlorine compound, N-N'-dichloroazodicarbonamidine (azochloramide), in contaminated and infected wounds. Azochloramide has been the subject of a few papers during 1935 and 1936. It possesses bactericidal properties of a high degree, but it is peculiarly inert against organic matter. It is the least irritating chlorine compound so far produced for surgical purposes. Azochloramide was used as an oily solution of triacetin 1:500 in all cases except for irrigation in empyema, when saline concentrations of 1:1,666 and 1:3,300 were believed to favour more ready absorption from the pleural cavity. There is evidence to indicate the triacetin solution is removed rather promptly, however. Young does not mention any deduced values from the use of the two saline concentrations. The value of azochloramide was judged by comparing a similar number of cases treated before this new chlorine compound was available, termed respectively control and experimental cases.

Identical incisions were made in operations for hydronephrosis, pyonephrosis and nephrolithiasis. Ten control and 7 experimental cases are compared. All cases were drained. The control cases with pre-operative positive urine cultures were irrigated with saline, Dakin's or mercurochrome solutions when infection became evident. The experimental cases with pre-operative positive urine cultures were treated by filling the drainage tube with azochloramide, beginning 24 hours after operation. Of the 10 controls 7 had positive urine cultures of *Staph. aureus* (4), *B. coli* (2), and *Staph. albus* (1). They healed in an average of 52 days. Of the 7 experimentals all had positive urine cultures of *Staph. aureus* (2), *B. coli* (3), non-haemolytic streptococcus (1), and *B. proteus* (1). Five of the 7 experimentals remained sterile and healed in an average of 15 days; 2 had perinephric abscesses in which the healing time averaged 30 days. Apparently, the azochloramide solution is capable of preventing infection in contaminated wounds.

In empyema, 7 controls and 6 experimentals were compared. The routine was aspiration until optimum time for surgical drainage. On the second day after drainage the cavity was filled with Dakin's or either of the two azochloramide saline solutions every four hours. The drainage tube was closed off for one hour, and then suction was applied. The 7 control cases were infected with *Pneumococcus* I (3); *Pneumococcus* IV (3), and *S. haemolyticus* (1). The cavities were treated as follows; closed drainage (3); rib-resection after closed drainage (3); primary rib-resection (1). They healed in an average of 83 days. The 6 experimental cases were infected with *Pneumococcus* I (1); *Pneumococcus* II (1); *S. haemolyticus* (2); anaerobic streptococcus (1), and *Myco. tuberculosis*, *Staph. aureus* and *B. pyocyaneus* (1). The cavities were treated as follows; closed drainage 2; primary rib-resection 3; and the one with triple infection finally by thoracoplasty. Two were irrigated with the 1:1,666 and 3 with the 1:3,300 solution. These 5 healed in an average of 41 days. The discharge from the experimentals was relatively much thinner in quality. It was possible to control the *Staph. aureus* with azochloramide solution and the *B. pyocyaneus* with 0.5 per cent acetic acid, but either one of the organisms was constantly present with the tubercle bacillus.

In infection with coincident diabetes, it is more difficult to draw conclusions because of the distinctly individual nature of each case. Eight controls healed in 87 days; 9 experimentals treated with packing every 24 hours healed in 64 days, both after amputations of one toe. In 5 controls with diabetes and carbuncles of an average diameter of 6 cm. treated with Dakin's solution the average healing time was 45 days; in 5 experimentals, with the same locations, of an average diameter of 8 cm. treated with daily packings the average healing time was 29 days.

The author also cites other cases of debridement in traumatic injuries packed with azochloramide in 1:500 triacetin, and the satisfactory results obtained in infected post-operative abdominal wounds with like results, and of bone infections, in which, however, the results were not so happy. Young allows full value to Dakin's solution in removal of necrotic tissue.

FRANK DORRANCE

Use of Urea to Stimulate Healing in Chronic Purulent Wounds. Robinson, W., *Am. J. Surg.*, 1936, 33: 192.

The author's interest was aroused after having used allantoin for a similar purpose. Allantoin is claimed to be one of the beneficial agents in the surgical use of maggots. The beneficial action of urea depends upon the stimulation of indolent tissues to produce granulation tissue

and a more abundant blood supply. Urea readily permeates the membrane of all cells. He cites a number of case reports to show rapid healing in such lesions as osteomyelitis of the femur, gangrene after frost-bite, cellulitis, abscesses of limbs and trunk, infected burns and varicose ulcers. The author states that urea is active only during the time it is in contact with the affected part, and that healing is evident by 72 hours after the commencement of treatment. A 2 per cent solution in sterile, cold distilled water has been found to be of most practical value, although a 10 per cent solution has been used in resistant cases. He has used it as a "hot soak" for one-half hour three or four times a day; as thoroughly saturated moist compresses loosely applied and covered with oiled silk or waxed paper; by syringing into sinuses or inaccessible parts and changing the dressing as indicated; as a bath of 0.25 per cent; and as a 15 per cent ointment in vanishing cream or other greaseless ointment base.

FRANK DORRANCE

Anæsthesia

The Meaning of the Phrase "A Good Anæsthesia". Charles, R. L., *Anæsthesia & Analgesia*, 1936, 15: 206.

The author defines the phrase in his presidential address at the Southern Medical Association Week in St. Louis, Miss. In so doing he realizes fully the three individuals directly affected, the patient, the surgeon and the anæsthetist. Some patients wish to go to sleep quickly or to leave their room in an unconscious state, others wish to avoid nausea, and mostly everyone wishes to be assured of awakening with the promise of better health in the future. The surgeon wishes to perform freely and fully his work without having to give thought to the patient's condition and to be assured of as little after-effect as possible; sometimes he does not realize these two states are not compatible. The anæsthetist wishes to avoid undue apprehension on the part of the patient. The author likes to make an appraisal of the risk the evening preceding operation. He believes it to be his duty to go over the case-record and to have a professional visit at the bedside. Fear allayed prevents depletion of the alkali reserve and lessens the likelihood of shock. The pre-operative sedative dose can be estimated at this visit or early in the morning. The author dislikes routine orders. He gives his anæsthesia according to the "Law of Anæsthetic Accommodation". The concentration of the drug administered is more often responsible for tissue injury than the length of the anæsthesia. Statistics are more often the measure of the

physician than of the drug. All anæsthetics are potentially dangerous, and particularly so in the hands of the one who is afraid or is over-confident.

FRANK DORRANCE

Evipal Anæsthesia: Résumé of 1,000 Cases. McNelis, P. J., *Anæsthesia & Analgesia*, 1936, 15: 199.

The author gives his experience as a private anæsthetist with evipal in a service where minor surgery of the traumatic type is of routine nature.

In traumatic surgery one usually finds a patient with a full stomach, moderately shocked, and in dread of the loss of his earning ability. These patients like evipal because of its lack of post-operative nausea and vomiting and the feeling of comfort and diminution of pain which follows.

McNelis was able to obtain fully satisfactory anæsthesia in such lesions as debridement of burns, suturing of wounds, drainage of abscesses, dilatation and enretage, radium implantation in the cervix, enucleation of eyes, cystoscopies, bronchoscopies, hæmorrhoidectomies, pelvic examinations, skin grafts, facial surgery, amputation of digits, to supplement spinal anæsthesia and all types of dental surgery. Injections of morphine and atropine, 45 minutes to one hour prior to tonsillectomies, reduction of fractures and appendectomies, gave more satisfactory conditions for the necessary procedures. In rib-resection, in minimal doses, repeated, with due respect to inhibited respirations, evipal anæsthesia was ideal. The use of evipal does not do away with the need of an anæsthetist at an operation. It has been found advisable to have a carbon dioxide and oxygen apparatus at hand, as well as coramine and so forth. The dose in children of 4 to 7 years was generally 2 to 3 c.c. He found 5 c.c. to be the maximum dose in children under 12 years of age. In males from 12 to 16 years post-operative restlessness was common until the dose had been increased to practically adult limits; adolescents have a high tolerance for barbiturates. The maximum dose given in this series was 4 injections of 10 c.c. each of the 10 per cent solution.

The author believes that evipal has a distinct place in our list of anæsthetics. It is best suited to the realms of minor surgery of traumatic origin. It should not be allowed to take a place with those accepted drugs whose qualities have earned them their place in the realms of major surgery. He does not believe it will come to act as a "pinch-hitter" in basal anæsthesia, nor to supplement spinal anæsthesia.

FRANK DORRANCE

Dr. Hotson first attended the East Zorra school and then the Rotho school, both in Oxford County. Later, he went to the Baptist Literary Institute at

Woodstock. After completing his course, he taught school for about six years in Oxford County before going to Toronto Normal in 1874. When he completed his year there he went to London as principal of the then St. George's School, and the next year to the old Union School in London.

In 1878, Dr. Hotson joined the teaching staff of the London Collegiate Institute as a science teacher and it was while teaching there, he took his medical course and was the second student to enroll in the medical school at Western University at that time. He received his medical degree in 1889. During his last two years, before he stopped teaching, with the permission of the Board of Education he lectured in biology to the medical students. That year he came to Parkhill and took over Dr. Owen's practice. Dr. Hotson was a member of the Microscopic Society in London, which later brought Dr. A. B. MacCallum from Toronto to London to give them a course in bacteriology. This was the first bacteriology course given in London.

He married Miss Annie Jones, of Ailsa Craig, in 1870. She died in 1896. Dr. Hotson leaves one daughter, Miss Aletha Hotson, of Parkhill, high school teacher; one son, Arthur E., a chemical engineer, of Shreveport, La.; a brother, Dr. John Hotson, Vancouver, and a sister, Mrs. Mary Hill, London.

Dr. Wray Devere Marr Lloyd died, as the result of an accident, on June 2, 1936, at Rio de Janeiro, Brazil, where he was prosecuting studies on yellow fever. He was thirty-three years old.

Dr. Lloyd was born at Collingwood, Ont., and was a graduate of the University of Western Ontario (1920). After graduation he spent three or four years at the University of Toronto, doing research work at the Banting Institute, where he was associated with Sir Frederick Banting and Prof. Oskar Klotz. He then went to the Rockefeller Foundation in New York and while there discovered a preventive for yellow fever. Both he and Dr. S. F. Kitchen, another Western graduate, were bitten by monkeys and contracted the disease.

Being immune from yellow fever after once being sick with it, Dr. Lloyd was sent to Africa, and later to South America by the Rockefeller Foundation, to continue his studies of the disease where it is most commonly experienced. Two months before his death, he returned from an eight-month sojourn in the jungle of South America securing samples of blood from the natives for test purposes.

Dr. Lloyd was a brilliant student and exceptionally thorough, and his death is a distinct loss to medical science.

He is survived by his widow, his parents, Mr. and Mrs. C. W. Lloyd, of Toronto, and a sister, Marie.

Dr. James Edward Lovering, of Lethbridge, Alta., died on August 11, 1936. James Edward Lovering was born at Coldwater, Ont., on November 5, 1871, the son of the late John Lovering and Mary Lynch. He became a school teacher as a young man and taught for nearly 12 years in the interior of British Columbia, spending considerable time at Revelstoke. Returning east he graduated with a medical degree from McGill University in 1908 and in the same year came to Magrath where he practised medicine for three months. He moved to Lethbridge in the fall of 1908, practising his profession continuously until June of this year when he retired.

At the time of his death Dr. Lovering was chairman of the Lethbridge public school board. Education had long been one of his chief interests and he had served on the local board for many years. He

was also active in southern Alberta and provincial educational circles.

Dr. Lovering acted as surgeon to the Royal Canadian Mounted Police in Lethbridge continuously from 1921 until June of this year when his health failed. He was named a coroner for his district many years ago.

Dr. Lovering was married in Lethbridge to Bessie Cronkhite soon after coming to the city. One daughter, Mrs. Bessie Marie Samson, of Lethbridge, was born to this union. Mrs. Lovering passed away in 1911, and in 1913 Dr. Lovering married Sadie M. Greenaway, who survives.

Dr. Amedée Marien, of Montreal, surgeon-in-chief of the Hôtel-Dieu, and a former professor in the University of Montreal, died on September 1, 1936, at the age of seventy-one.

Dr. Marien was born in the village of Rivière des Prairies on the Back River. He studied first at l'Assomption College. After graduating there he studied medicine at the Ecole de Médecine Victoria, which later became the faculty of medicine of Laval University, eventually becoming linked with the University of Montreal. He then went to France and studied for some years at the Institut Pasteur. He introduced here on his return many methods then practised in European hospitals. While in France he studied under such prominent French medical leaders as Wineberg, Brault and Legueux, at a time when France was leading the world in medical progress after Pasteur's discoveries. He was one of the first members of Montreal's old Société de Médecine, which later became the Union Médicale du Canada and was one of the founders of the Association of French Speaking Doctors of North America.

Dr. Arthur Dalton Smith, of Mitchell, Ont., died on August 30, 1936. He was born in 1858 and a graduate of the Medical Faculty, Trinity University (1882).

Lieut.-Col. A. M. Warner. It is with deep regret that we note the death on July 18th of Lieut.-Col. A. M. Warner, B.A., M.D., C.M., Vancouver, after an illness of nine months. Born at De Lewisville, Ontario, Dr. Warner was educated at Cayuga, and graduated from Queen's University, taking his degree in Arts in 1910 and in Medicine in 1912. He became an intern at the Vancouver General Hospital and entered private practice in Vancouver in 1913. He was a valued member of the Vancouver Medical Association and the British Columbia Medical Association.

In 1916 Dr. Warner went overseas with the R.A.M.C. and was appointed O.C. of the Carrier Depot Hospital at Dar-es-Salaam, in German East Africa, which he had built and organized. During his command there 13,000 patients were admitted. He was then sent to Lindi to organize a hospital on similar lines, but became dangerously ill with malaria and was invalided to England. Because of recurrent attacks of malaria he was unfit for service abroad and was attached to Balloon Squadron, Outer Defences of London, as M.O. for a year.

On his return to Canada he rejoined the C.A.M.C. and became attached to the 18th Field Ambulance. He was Officer Commanding the Field Ambulance from 1926-1930, and was appointed Deputy District Medical Officer of Military District No. 11 for four years. He was also O.C. of the Casualty Clearing Station.

Lieut.-Col. Warner was mentioned in despatches by General Van de Venter, and qualified for the Long Service Medal in the C.A.M.C.

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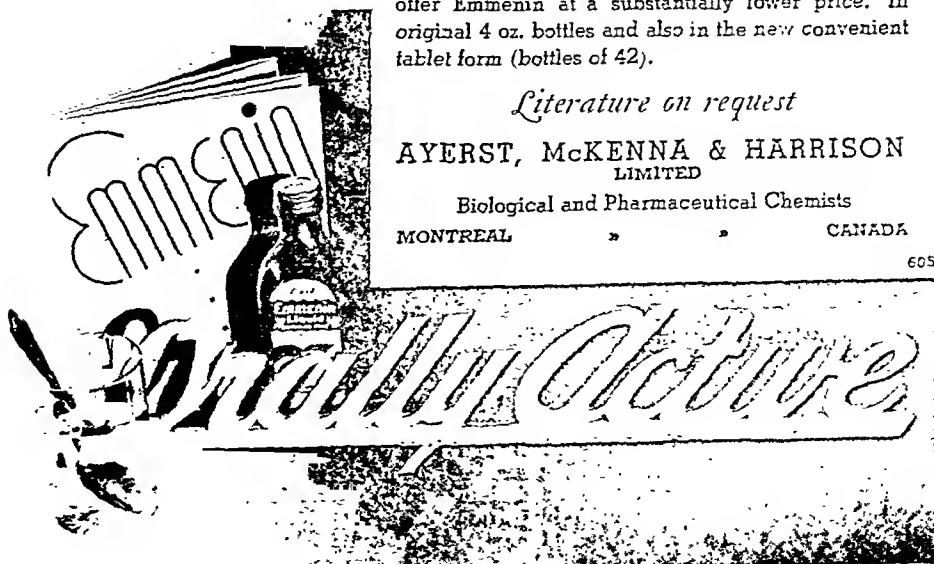
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News Items

Great Britain

The Bureau of Human Heredity.—The object of this Bureau is collection on as wide a scale as possible of material dealing with human genetics. Later, the tasks of analysis of material and distribution of the information available will be added.

The Bureau is directed by a Council representing medical and scientific bodies in Great Britain. It is affiliated to the International Human Heredity Committee, which ensures cooperation in all areas where research is proceeding.

The Council would be grateful to receive all available material from institutions and individuals, furnishing well-authenticated data on the transmission of human traits whatever these may be. Pedigrees are particularly desired; twin studies and statistical researches are also relevant. As research workers and others who send in material may in some cases wish to retain the sole right of publication (or copyright) those who so desire are asked to accompany their material with a statement to that effect.

Material should be given with all available details in regard to source, diagnostic symptoms and the name and address of the person or persons who vouch for accuracy. All such details will be regarded as strictly confidential.

Reprints of published work would be most acceptable. Further, many authors when publishing material may also have collected a number of pedigrees which they have been unable to reproduce in detail. It is the object of the Council that such records, by being included in the Clearing House, should not be lost.

Those wishing for a copy of the Standard International Pedigree Symbols may obtain one from the office.

Announcements in regard to the services undertaken by the Bureau will be published from time to time.

Chairman: R. Ruggles Gates. *Executive Committee:* R. A. Fisher, J. B. S. Haldane, E. A. Cockayne, J. A. Fraser Roberts, L. E. Halsey (Hon. Treasurer), C. B. S. Hodson (Hon. Gen. Secretary). (115, Gower Street, London, W.C.1, England.)

Alberta

The Alberta Government has indicated that they will pay basic dividends to all eligible covenanters in a few weeks, the amounts and dates are still unfixed. It has been hinted that medical men will be asked to accept a portion if not all their fees for the care of those on relief in credits. If these credits have 100 per cent purchasing power for Alberta products the results may not be so serious. G. E. LEARMONTH

British Columbia

Work is being started on the new wing of the Kings' Daughters Hospital at Duncan, which will increase the building's capacity from 60 to 85 beds. The two-storey addition will contain men's medical and surgical wards on the ground floor, an Indian section with wards for men, women and children, and a modern diet-kitchen. The second floor will be occupied by private and semi-private rooms, a children's ward and nurses' dining-room.

Dr. S. C. Peterson, formerly of Winnipeg, has been appointed by the Provincial Government as director of venereal disease control for British Columbia. A reorganization of this department of the Provincial Health Department is contemplated, and the government

has increased its appropriation for venereal disease control from \$30,000 to \$45,000.

Dime-in-the-slot "blood-pressure machines," such as have been operating in amusement-parks and on street-corners in various cities of the United States, and which have been banned—if we are not misinformed—in some places, have made their appearance on Vancouver streets. Much interest has been shown by the lay-public and patronage of this new "amusement device" has been generous. To protect himself from the charge of practising medicine without a license the concessionaire has set up signs reading, "Attendant is forbidden to diagnose, prescribe or treat under any circumstances. The only purpose of this machine is to let you read your blood pressure and nothing else." The medical officer of health is quoted in the press as stating that he cannot see that it will do much harm, and it may possibly do some good.

D. E. H. CLEVELAND

Manitoba

A combined meeting of the North-western District Society and the Brandon and Medical District Society was held at Clear Lake on September 9th. The principal speakers were Dr. Gordon Fahrni, of Winnipeg, and Dr. F. R. Bird, of Boissevain.

At the time of writing about 80 cases of anterior poliomyelitis have been reported this fall, chiefly from south-western Manitoba. The epidemic originated about Boissevain, and deaths have been reported from that town, Morden, and Portage la Prairie. Dr. M. R. Elliott, D.P.H., of the Department of Public Health, is working on the field and giving assistance to the local doctors. All the municipalities in which more than four or five cases have been reported have agreed to provide free diagnosis and treatment. Supplies of convalescent serum are being sent out as required from the provincial bacteriological laboratory at Winnipeg.

Dr. S. C. Peterson, Director of Social Diseases for the Manitoba Department of Health and Public Welfare, and clinical instructor in these diseases in the Faculty of Medicine, University of Manitoba, has resigned to become Director of Social Disease Control for British Columbia, and left on September 15th to assume his new duties.

On September 17th, at the Fort Garry Hotel, Winnipeg, a dinner was given in honour of Dr. R. G. Inkster, late Professor of Anatomy in the Faculty of Medicine, University of Manitoba, who will leave shortly to assume a position as Anatomist in Trinity College, Dublin. Dr. J. A. Gunn, Professor of Surgery, was in charge of the arrangements. ROSS MITCHELL

New Brunswick

Dr. S. S. Skinner has retired, as from September 1st, from the position he has held as chief medical officer of the Lancaster Hospital under the Department of Pensions and National Health. Dr. H. D. Reid, Federal Quarantine officer, at Partridge Island, Saint John, has been transferred to Lancaster Hospital to succeed him. Dr. Skinner has been identified with the Lancaster Military Hospital since 1919 and has been Medical Director of the Hospital since 1924. He was for many years an attending physician at the Saint John General Hospital. He served overseas, and his many friends wish him a pleasurable retirement.

Dr. C. O. McKay has been appointed assistant in the Department of Physical Medicine, at the Saint John General Hospital.

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Dr. A. L. Donovan, of the Department of Medicine at the Saint John General Hospital, has returned home following a month's post-graduate course at McGill University.

The program for the meeting of the New Brunswick Medical Society at Bathurst is complete. The scientific program includes both Maritime and Upper Canadian speakers. The North Shore Medical Society are hosts this year of the Parent Society.

Dr. D. C. Malcolm, Dr. V. D. Davidson, both of Saint John, and Dr. E. T. Kennedy, of Sussex, N.B., have returned from Europe, which they visited in connection with the Vinny Pilgrimage. A. STANLEY KIRKLAND

Nova Scotia

The fifteenth session of the annual Dalhousie Refresher Course was held in Halifax, August 31st to September 1st, with a record attendance. Since its inception this post-graduate course, presented by the Medical Faculty of Dalhousie University and her associated hospitals, has grown in popularity with the Nova Scotia medical profession. This year it was held in conjunction with the annual meeting of the Nova Scotia Medical Society. The registration mounted to 183, of whom more than 100 were from outside Halifax. This was far in excess of the Medical Society registration. It represents about 40 per cent of those in active practice in the province! Than this figure no higher compliment could be paid both to the Refresher Course and to the profession that took advantage of it.

The program followed the general plan of previous years. The mornings were devoted largely to hospital clinics, conducted by staff members and guest clinicians; afternoons to lectures. Symposia, prominent features of the past two sessions, were omitted from this course, but through the week ran a theme, the subject of infant and maternal welfare. It has been the policy of the Refresher Course Committee to present informal addresses of a teaching nature rather than the more polished, but less engaging, presentation of manuscripts. This was carried out in every instance.

Dr. C. H. Best, of Toronto, told the story of protamine-insulin and its place in diabetic therapy. Dr. Channing Frothingham, Physician-in-Chief at the Faulkner Hospital, Boston, Mass., in two lectures, took up the "Organization of a community hospital for the best of service" and "The present status of endocrine therapy". Dr. Frothingham's first talk was of real value to those vitally interested in the many small hospitals throughout Nova Scotia. His refreshing conservatism in endocrine therapy was a tonic to many suffering from an inability to reconcile clinical results with drug agents' perorations.

Dr. J. H. Couch, Fellow in Surgery, University of Toronto, presented ingeniously and instructively a demonstration of local anaesthesia, Kirchner wire, and the walking cast in the treatment of fractures. As his second lecture Dr. Couch took up the injection treatment of varicose veins and hemorrhoids. Diagnosis and treatment of enlargements of the superficial lymph glands and, again, of conditions associated with jaundice were the subjects of Dr. Ray F. Farquharson, Professor of Therapeutics, Toronto University. Dr. Farquharson's presentations were lucid, practical and most comprehensive.

Maternal and infant welfare was considered in its many phases by Dr. A. L. MacLean, Epidemiologist of Dalhousie University. Dr. Atlee, Professor of Gynaecology. Dr. Maclellan, Professor of Obstetrics, and Dr. Wiswell, Associate Professor of Paediatrics. Dr. Johnston, Roentgenologist to the Victoria General Hospital, discussed, in two lectures, the principles and practice of radiation therapy. Dr. Muir, head of the Department of Anaesthesia took up spinal and intravenous anaesthesia.

Clinics were presented by each of the services of the Victoria General Hospital, by the Children's Hospital Staff and the Staff of the Dalhousie Health Clinic. There were lectures and demonstrations by Dr. Ralph Smith's Department of Pathology. Special clinics were given by Dr. Frothingham and Dr. Farquharson.

The Refresher Course Committee with whom lay the responsibility for the planning and organization of the course consisted of Dr. Hugh W. Schwartz (chairman), Drs. T. M. Sieniewicz, N. H. Gosse, G. A. Winfield, Victor Mader, Gordon Wiswell, C. W. Holland, J. A. Noble, Ian Macdonald, and Dean Grant of the Medical School.

That the provincial government take full responsibility for the tuberculous sick of the province was the tenor of a resolution passed by the Union of Nova Scotia Municipalities at their annual meeting at Digby. The financial burden in the case of patients without means of support was, they felt, more than several of the municipalities could bear.

The annual golf tournament of the Nova Scotia Medical Society was won by Dr. P. A. MacDonald, of Halifax. Dr. J. W. Merritt, of Halifax, was low net, while Dr. W. G. Colwell, also of Halifax, had the unique glory of a hole in one.

Dr. C. J. W. Beekwith (Dal. '27), assistant superintendent of the Nova Scotia Sanitarium has gone to the University of Toronto, where he will spend the next year in the study of hygiene and public health.

Returning from two years' post-graduate work in New York, Dr. Carl F. Messenger, son of Dr. F. S. Messenger, will resume his practice in the Annapolis valley.

Senior among those registered at the Dalhousie Refresher Course was Dr. M. A. Curry, Professor of Obstetrics and Gynaecology at the Dalhousie Medical School from 1888 to 1921. Dr. Curry is active and well in his eightieth year.

Dr. B. F. Miller, New Waterford, has sailed for Europe where he will spend the next year in post-graduate study. Mrs. Miller and their young son accompany him. ARTHUR L. MURPHY

Ontario

Dr. Charles H. Gundry, who has been on the staff of the Toronto Psychiatric Hospital, has received a Commonwealth Fund Fellowship, which carries with it an appointment at the Child Guidance Clinic, Cleveland.

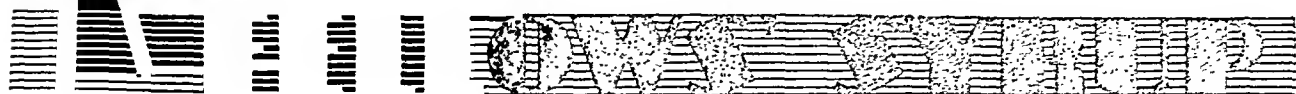
The Ontario Department of Health has issued a Bulletin notifying all municipalities that, after September 1st, they will have to pay 25 per cent of the cost of insulin supplied free to indigents.

Dr. E. L. Williams, of London, has been elected President, for 1936-1937, of the Medical Alumni of the University of Western Ontario.

Contracts totalling over \$25,000 have been let for the erection of a nurses' home at the Kitchener-Waterloo Hospital.

Professor H. B. Maitland, a graduate in medicine of the University of Toronto of 1916, and now of the University of Manchester, has been appointed Dean of the Medical School in succession to Professor H. S. Draper, who was, at one time, on the staff of the University of Toronto. J. H. ELLIOTT

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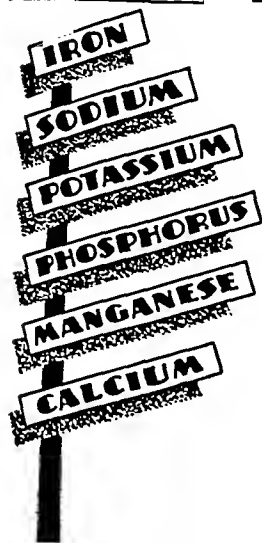
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Quebec

It has been customary for the past few years to hold a St. Luke Day's Service in St. George's Church, Montreal. This service has been conducted by the rector, the Ven. Archdeacon Gower-Rees, who also preached the sermon. The lessons were read by medical men, usually by Dr. W. W. Francis, the late Dr. Campbell Howard, and Dr. Frank Patch, and other medical men acted as sidesmen. This year the service will be held on the morning of October 25th and will present a new feature in that a medical man will preach the sermon. Dr. G. N. Paterson-Smyth, the son of a former rector of the Church, will be the special preacher. His subject will be "Fear and Courage".

Book Reviews

The Practitioner's Library of Medicine and Surgery. Vol. 10, Dermatology and Syphilology. 1043 pages, illustrated. Price \$10.00. D. Appleton-Century Co., New York and London, 1936.

The preceding nine volumes of this series were reviewed in the December, 1935, and June, 1936, issues of the *Journal*.

In the section of dermatology, the physical and mental constitutional habits, the blood chemistry, and the occupation of the patient have been given more than usual consideration. In common with other works a good description of the anatomy and physiology of the skin is given. Diagnosis is approached from three angles, namely, the pathological, the specialist, or area of distribution, and that of the general practitioner, or progress. There is up-to-date evaluation of the various drugs used, externally and internally. Enesol is recommended in lichen planus for its symptomatic and curative value. The use of the monopolar diathermy current is replacing to a large extent the use of caustics; x-ray treatments are given the prominence they deserve. Fungous infections, superficial and deep, are thoroughly handled; the importance of residual foci, such as onychomycosis, have not been generally accorded by public health authorities and others the prominence they warrant. The use of photographs of microscopical slides would have enhanced the practical value of this chapter. The roles of the calcium-potassium ratio of the blood serum, the pathological blood sugar curve and the blood uric acid content are stressed in the intertriginous and eezematous states. The Urbach propeptone manner of diagnosing food hypersensitivity is given favour over the Vanderbilt Clinic Diets. The discussion of the seborrhoeic diathesis is indeed refreshing in this day of commercially-lauded but hopelessly ineffectual "antiseptic" treatment.

The section of syphilis is marked by the insistence on dark field examination as the primary requisition in diagnosis. In the author's opinion continuous treatment for the first year by an alternate series of ten injections each of arsphenamine, and a heavy metal gives the highest percentage of clinical and serological "radical cure". And, "in view of the frequency of relapse or progression in any stage of the infection, no syphilitic patient should ever be dismissed as cured". He attempts to define immunity to the *Treponema pallidum*, and in this regard he places pregnancy as the factor of greatest efficiency; early treatments, irregularly given, are the most harmful factor. They prevent the development of tissue response. His analysis of the Wassermann-fast state is stimulating. He would have all Wassermann tests made on the titration basis and base improvement by such. Wassermann "fastness" at the completion of six months of treatment means that ocular or neurosyphilis was present before treatment began, and our attempts should also be directed immediately to their arrest. This volume presents the 1936 analysis of dermatology and syphilology and should be of interest to every practitioner.

Diseases of the Respiratory Tract. By various authors. 418 pages, illustrated. Price \$6.25. W. B. Saunders, London and Philadelphia; McAlush & Co., Toronto, 1936.

This volume covers a wide range of subjects in the field of respiratory diseases. It is a record of newer viewpoints in this important field as given in a series of lectures by outstanding authorities at the Eighth Annual Graduate Fortnight in New York. Among the subjects treated are Allergy in Relation to Respiratory Diseases; the Common Cold; Diseases of the Larynx; Trachea and Bronchi; Bronchoscopy; Pneumonia; Bronchiectasis; Pneumococcosis; Tuberculosis; Emphysema and Carcinoma of the Lung. The discussion of the newer contributions to our knowledge in these fields is presented in a critical and very readable fashion.

The present status of allergy in relation to Hay Fever and Asthma, and the evaluation of skin tests is particularly well outlined by Ramirez. Jackson, in his usual lucid style, covers the field of bronchoscopy. Tuberculosis is discussed from the point of view of its evolution and immunity reactions as seen in the human individual at various ages. There are many valuable facts and much sage wisdom in these two chapters. The importance of the industrial hazard in relation to silica dust and its association with tuberculosis is discussed under pneumoconiosis by Gardner. Yandell Henderson has contributed an intriguing chapter on the physiological factors in massive collapse of the lung.

This is a book which can be profitably read and used for reference both by the internist and the general practitioner.

The Common Cold and Influenza and their Relationship to other Infections in Man and Animals. J. E. R. McDonagh, F.R.C.S. 148 pages. Price \$3.75. Wm. Heinemann, London; Macmillan, Toronto, 1936.

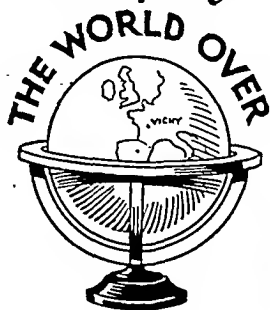
As the title indicates the author sets out in an attempt to correlate rather than differentiate various types of infectious disease. He develops the theory that *B. coli communis* in the intestinal tract is the common parent of a host of other organisms. These organisms, he believes, arise as mutation forms of *B. coli* and invade various regions of the body, causing a wide variety of infections including the common cold and influenza. The author does not accept the recent work on filterable viruses in the production of the latter diseases except in that the viruses are mutation forms of *B. coli communis*.

The book is certainly unorthodox, and one feels that few bacteriologists and epidemiologists will agree with the author's viewpoint. Dr. McDonagh is rather too dogmatic in his assertions and too far-reaching in his conclusions from the amount of clinical and experimental data presented. A perusal of this volume however gives one food for thought in the explanation of the factors which influence the incidence of epidemic disease.

Exophthalmic Goitre and Its Medical Treatment. Israel Bram, M.D., Medical Director, Bram Institute for Treatment of Goitre, Upland, Pa. Second edition, 456 pages, illustrated. Price \$7.00. C. V. Mosby, St. Louis; McAlush & Co., Toronto, 1936.

In 1920 we had the pleasure of reviewing Dr. Bram's work, *Exophthalmic Goitre and Its Non-Surgical Treatment*, with favourable comment. Since that time the author has continued his interest in the subject, and with much more extensive experience and observation has written this volume, practically a new work. He makes it quite clear that he believes Graves' disease is not thyrogenous in origin, but is a neuroendocrine dysfunction, with or without hyperplasia of the thyroid gland, and that psychic trauma is the most evident provocative factor in its causation. His wide experience leads him to believe that thyroidectomy removes only a result of the disease, not the cause, and hence it only ameliorates the symptoms. He states the indications for thyroidectomy, but considers that they are present in only about 2 per cent of all patients. Toxic adenoma, clearly a neoplastic condition, requires surgical treatment, but this disease is not in-

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cluded. He discusses only Graves' disease. In his preface he says "The more competent the surgeon, the greater the emphasis on pre-operative and post-operative medical treatment as vital to the patient's welfare, until, when we examine the contributions of leaders in this field, we find skepticism respecting the adequacy of thyroidectomy in the average case of Graves' disease". He even suggests that the time has come for the profession to render obsolete the orthodoxy of an attack on the thyroid as a treatment of the disease. He reports that he has followed up 2,600 cases treated medically, and after three to twenty years he finds 90 per cent are entirely well. The remainder are relatively well, and most of the 10 per cent in this group are enjoying complete social and economic usefulness. Outside the section on treatment there is a full presentation of the various theories of the etiology of the disease, its symptomatology, diagnosis, types, laboratory tests, and a chapter on prevention.

The Relief of Pain. Harold Balme, M.D., F.R.C.S., D.P.H. 392 pages. Price 12s. 6d. J. & A. Churchill, London, 1936.

Some seventy-five years have passed since John Hilton delivered his famous lectures which in book form are a classic that all students and practitioners should read. Time had only served to emphasize the value of his observations upon rest as an essential factor in the relief of pain. In recent years investigation and observation, both clinical and experimental, have added to our knowledge of the nature of pain, its pathways, whether visceral or referred, and variations in sensitivity.

Dr. Balme emphasizes that the first essential in the treatment of pain is a knowledge of its cause. After a discussion of the nature of pain, its problems and investigation, he has practical chapters on prevention, on pain from inflammation and from injuries, and then proceeds to pain in the various systems, skeletal nervous and circulatory, before taking up the subject of regional pain and therapy, both general and local. There is a valuable chapter for ready reference, listing analgesic drugs with their composition, therapeutic use, and dosage.

He has assembled in a critical study the preparations and physical methods available for the prevention and alleviation of pain, indicating their limitations and dangers. Throughout there appears evidence of wide experience, as well as of keeping abreast of every advance in this special field of therapeutics.

Surgical Pathology of the Gastro-Intestinal Tract.

Arthur E. Hertzler, M.D., Surgeon to the Agnes Hertzler Memorial Hospital, Halstead, Kansas. 311 pages, illustrated. Price \$5.00. J. B. Lippincott, Philadelphia, Montreal, and London, 1936.

This is one of an ambitious series of monographs on surgical pathology, written by one of wide experience in pathology as well as surgery and gifted with a facile pen. His story is most readable. The illustrations are outstanding, not alone from their excellence but also on account of the very effective use of insets. Frequently the main illustration depicts a gross specimen, with an inset of either a low or high power view, or both, of the topical lesion. Each chapter gives the author's views in no uncertain terms. In dealing with the relationship between gastric ulcer and carcinoma, a definite stand is taken against their frequent association. The subject material is well arranged and fairly complete. That most interesting, though rare, condition, adenoma of the pancreas, might well have been included.

This book should be of practical value not only to the surgeon but also to the internist. It is more clinical than pathological.

The Specificity of Serological Reactions. Karl Landsteiner, M.D., The Rockefeller Institute for Medical Research, New York. 178 pages. Price \$4.00. C. C. Thomas, Springfield and Baltimore, 1936.

The author brings together in this review the most recent concept of the chemical aspects of immunological reactions. The material has been arranged in more or less the same sequence as the development of the subject.

There are five main chapters, dealing with (1) The Serological Specificity of Proteins, (2) The Specificity of Cell Antigens, (3) The Specificity of Antibodies, (4) Artificial Conjugated Antigens, and (5) Chemical Investigations on Specific Cell Substances; Carbohydrates, Lipoids. The author draws liberally from his vast experience in this subject, and also includes abundant references to other workers in this field. A perusal of this work outlines the important part the application of chemistry plays in the field of immunology. From a knowledge of the chemical constituents of the various antigens specificity of reactions is now readily explained. A very comprehensive bibliography is given at the end of each chapter, enabling ready reference to any part of the subject. The text lacks no element of detail and yet it is written in a most readable fashion. This is a review from the pen of one of the most conversant workers in the problems of this subject and may be highly recommended. The printing and binding are of the usual high order.

Manual of Practical Obstetrics. O'Donel Browne, M.B., B.Ch., B.A.O., F.R.C.P.I., L.M., M.C.O.G., Assistant Gynaecologist, Sir Patrick Dun's Hospital, Dublin. 363 pages, illustrated. Price \$6.00. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1936.

The manual of practical obstetrics just been published by O'Donel Browne of Rotunda Hospital, Dublin, is a nicely bound, clearly written, well illustrated book. It is fashioned after Evans' Manual of Obstetrics, published in 1909, in that it is specially designed to suit the requirements of the undergraduate student and the general practitioner of medicine. The literature is well divided into chapters. The chapters upon normal labour, the toxæmias of pregnancy, puerperal sepsis, pelvimetry, and radiology in obstetrics contain a full description, concisely written. The chapters upon embryology or development, endocrine studies in obstetrics, development of the placenta, and the pathology of the placenta are too brief, and do not do justice to their importance in obstetrics. Posterior positions are also briefly dealt with, and many of the recent and valuable advances described in American literature are not mentioned. The book ends by giving an explanation of blood transfusion, and this, together with the subject of radiology in obstetrics, is new and of immense value. This publication can be highly recommended to the undergraduate student in medicine and also to the general practitioner, because many valuable points in the technique of obstetrics are emphasized.

The Extra-ocular Muscles. Luther C. Peter, A.M., M.D., Sc.D., Professor of Diseases of the Eye, University of Pennsylvania. Second edition, 351 pages, illustrated. Price \$4.50. Lea & Febiger, Philadelphia, 1936.

In this second edition Peter has followed the principles laid down in the first, so that the text has not been materially altered in fact or principle, though the advances of recent years have been included.

A chapter on operative technique has been added, and, whilst the author does not pretend to include all of the many excellent procedures of others, measures practised by himself and found to be satisfactory have been stressed. The book is well illustrated, and, as Peter from his vast experience in work of this kind can speak with authority, the book can be highly recommended.

Post Mortems and Morbid Anatomy. Theodore Shennan, M.D., F.R.C.S., Professor of Pathology, University of Aberdeen. Third edition, 716 pp., illustrated. Price \$9.00. E. Arnold & Co., London; Macmillan, Toronto, 1935.

The new edition of this splendid post-mortem reference book follows the same general outlines as the previous edition, beginning with a general statement concerning post-mortems, including a list of equipment. This is followed by a description of the performance of a post-mortem in great detail, including autopsy technique, and restoration. A scheme of examination of each organ and part of the body is presented and accompanied by a dis-

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CANADA

cussion of the various diseases of the part in question. The discussion of medico-legal examinations and reports is very good. A very complete manual which could well be included in the equipment of every autopsy room and kept there for ready reference.

Tuberculosis. Gerald B. Webb, M.D. *Clio Medica* Series No. 16. 184 pages. Price \$2.00. Paul B. Hoeber, New York, 1936.

This pocket-size volume is the sixteenth in the popular *Clio Medica* series of primers on the History of Medicine. The author covers in a concise authoritative manner the development of our knowledge of tuberculosis. The division of the subject matter into chapters dealing with various phases of tuberculosis makes the volume particularly valuable. The subjects treated are contagion, pathology, bacteriology, immunity, and treatment in their historical aspects. The book contains much useful historical data cleverly woven into an easily readable story of this important disease. There are a number of interesting illustrations, and an extensive bibliography.

Studies in the Psychology of Sex. Havelock Ellis. Four volumes. Price \$16.00 the set. Random House, New York; Macmillan, Toronto, 1936.

This well-known and monumental work by Havelock Ellis, previously restricted in its sale, now appears in popular form for general consumption. The topics discussed are the following: Vol. 1—The Evolution of Modesty; Sexual Periodicity; Auto-erotism; Analysis of the Sexual Impulse; Love and Pain; The Sexual Impulse in Women. Vol. 2—Sexual Selection in Man; Sexual Inversion. Vol. 3—Erotic Symbolism; The Mechanism of Detumescence; The Psychic State in Pregnancy; Eonism and other Supplementary Studies. Vol. 4—Sex in Relation to Society.

The author, in a lengthy preface, details the history of his work and the vicissitudes which it met with until now, when the change in outlook and opinion has rendered it possible to present it without fear of active opposition. He regards sex "as the central problem of life" and believes that "the question of sex—with the racial questions that rest on it—stands before the coming generation as the chief problem for solution". This is the *raison d'être* for the book. Whatever one may think as to the necessity of popularizing (and vulgarizing) information of the kind given in the book, and, in our opinion, it is hardly edifying for non-professional readers, yet there can be no doubt that it is of great value to the physician, lawyer, sociologist, ethnologist and educationist. The various subjects are dealt with in detail and with completeness, the arguments being supported by the testimony of physicians and patients, by case-reports and case-histories, and by quotations from poets, novelists and theologians. It would be hard to think of any point that has been overlooked.

Principles and Practice of Recreational Therapy for the Mentally Ill. John E. Davis, B.A., M.A., Senior Physical Director, Veterans' Administration Facility, Perry Point and William R. Dunton, Jr., Instructor in Psychiatry, The Johns Hopkins University, 197 pages. Price \$3.00. A. S. Barnes, New York, 1936.

The author defines recreational therapy as any free voluntary and expressive activity—motor, sensory, or mental, vitalized by the expansive play-spirit, sustained by deep-rooted pleasurable attitudes, and evoked by wholesome emotional release, prescribed by medical authority as an adjuvant in treatment.

Attempts to readjust mental patients are often frustrated by the intense preoccupation which the patient has with his own fantasies, delusional ideas, and feelings, which make it apparently impossible for him to become interested in the realities which surround him. Occupational therapy such as is outlined in this book is frequently exceedingly helpful in the attempts at re-education and re-socialization of these patients. This is well borne out by the favourable response of patients in those mental hospitals which have equipped themselves with facilities for recreational and occupational therapy.

After discussing briefly the various types and disease entities in this field, and indicating the major concepts involved in the process of re-education and re-socialization, the author proceeds to classify in considerable detail the various types of activities, formal and informal, exercises and games, which may be employed in this therapeutic endeavour with certain types of patients.

This book will certainly be a valuable aid to the physician who is specially interested in nervous and mental disease.

Nursery Education, Theory and Practice. William E. Blatz, M.A., M.B., Ph.D. and Dorothy Millichamp, M.A. and Margaret Fletcher, all of the St. George's School for Child Study, University of Toronto. 365 pages; price, \$3.50. Published by William Morrow and Co., New York, 1935.

Based chiefly upon their work at St. George's School for Child Study, the authors set out in a clear and logical manner the theory and methods used in the education of the young children under their care. The book is particularly satisfactory in that it gives not only the broad principles underlying the educational plan but also the detail of application. It is satisfactory to know that in Canada this most important subject of nursery schools is being studied, and that those directing the study are capable of passing on their experience in such a publication. Anyone who desires to have a definite guide in the training of young children will find it in this volume.

BOOKS RECEIVED

On Percussion of the Chest. Being a translation of Auenbrugger's Original Treatise. John Forbes, M.D. 31 pages. Price \$0.75. Johns Hopkins Press, Baltimore, 1936.

Williams' Obstetrics. Henricus J. Stander, M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Cornell University. Seventh edition, 1269 pages, illustrated. Price \$10.00. D. Appleton-Century, New York and London, 1936.

The Vegetative Nervous System. Wulf Sachs, M.D. 168 pages, illustrated. Price \$4.50. Cassell & Co., London; McAlash, Toronto, 1936.

Heart Disease and Tuberculosis. S. Adolphus Knopf, M.D., New York. 108 pages, illustrated. Price \$1.25. Livingston Press, Livingston, N.Y., 1936.

Contraception as a Therapeutic Measure. Bessie L. Moses, M.D. 106 pages. Price \$1.00. Williams & Wilkins, Baltimore, 1936.

A Diabetic Manual. Edward L. Bortz, A.B., M.D., F.A.C.P., Associate Professor of Medicine, University of Pennsylvania. 222 pages, illustrated. Price \$2.00. F. A. Davis, Philadelphia, 1936.

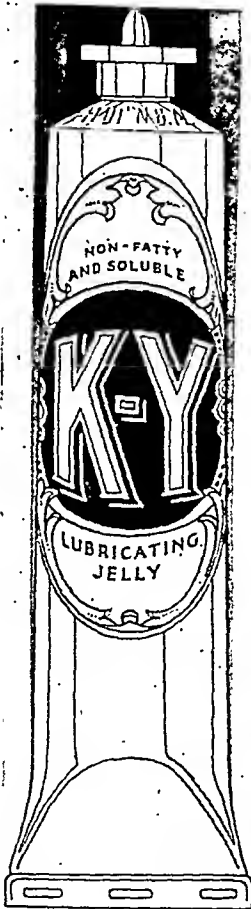
Chemical Procedures for Clinical Laboratories. Marjorie R. Mattice, A.B., Sc.M., Assistant Professor of Clinical Pathology, New York Post-Graduate Medical School of Columbia University. 520 pp., illustrated. Price \$6.50. Lea & Febiger, Philadelphia, 1936.

Research on the Low Potencies of Homœopathy. W. E. Boyd, M.A., M.D., Radiologist, Glasgow Homœopathic Hospital. 38 pages. Price \$0.75. Wm. Heinemann, London, 1936.

Textbook of Pharmacognosy. George E. Trease, B.P., Ph.C., F.L.S., Lecturer on Pharmacognosy, University College of Nottingham. Second edition, 671 pages, illustrated. Price \$6.25. Baillière, Tindall, & Cox, London, 1936.

Textbook of Neuro-Anatomy. Albert Kuntz, Ph.D., M.D., Professor of Micro-Anatomy, St. Louis University School of Medicine. Second edition, 519 pages, illustrated. Price \$6.00. Lea & Febiger, Philadelphia, 1936.

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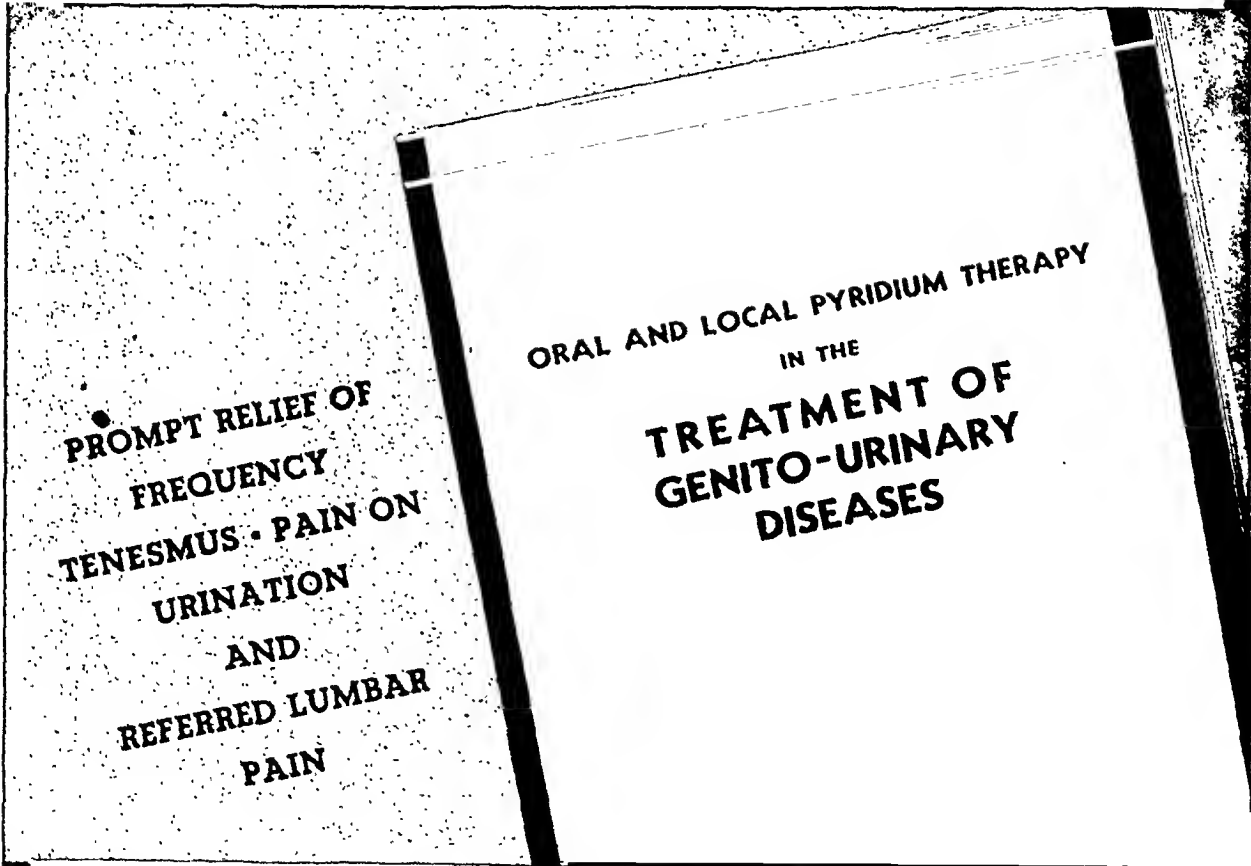
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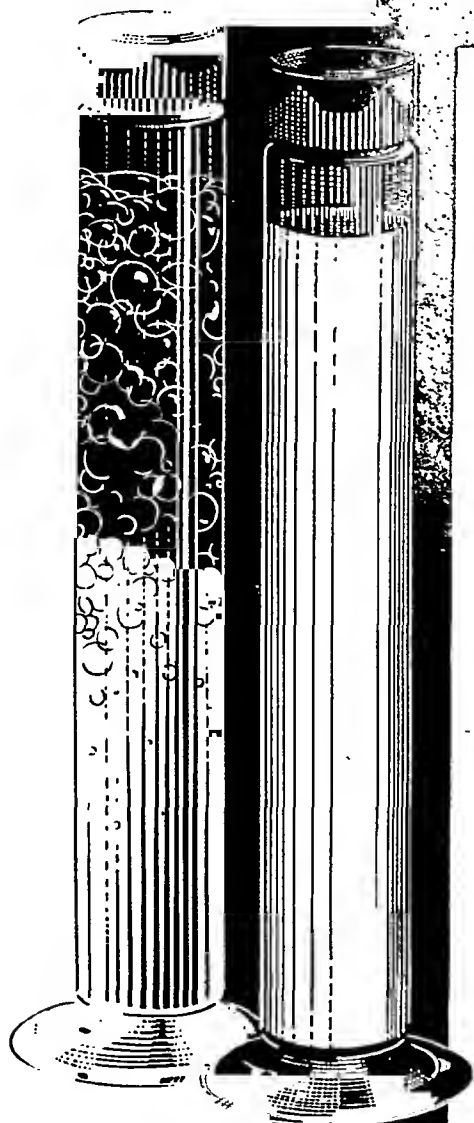
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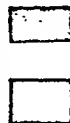
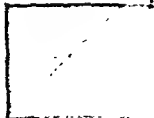


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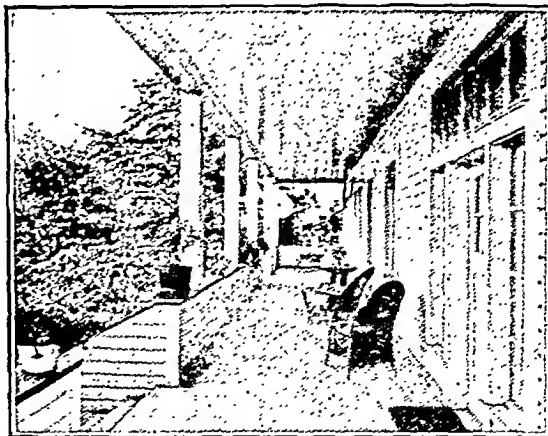
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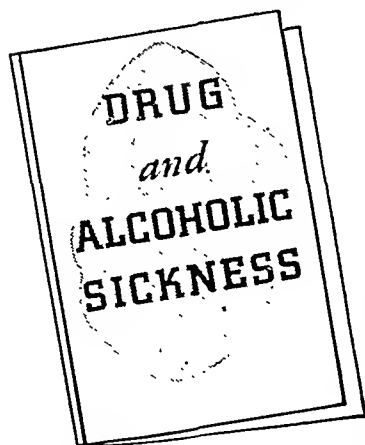
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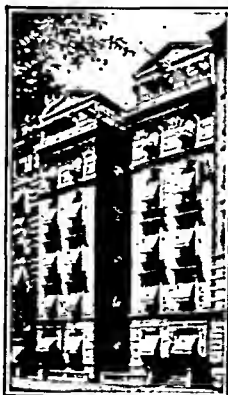
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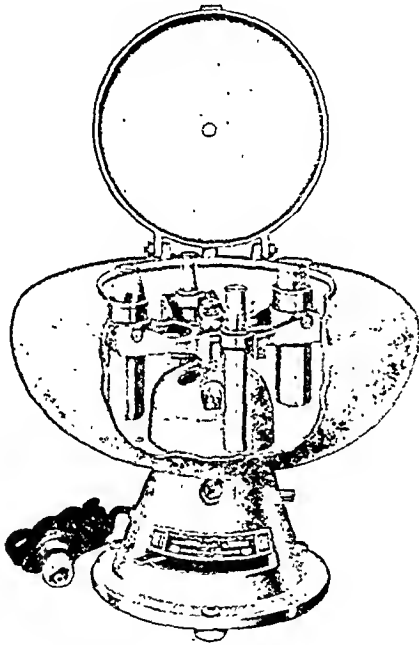
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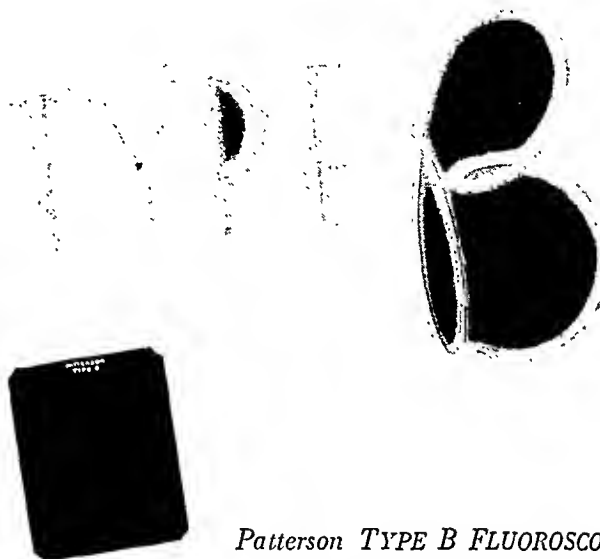


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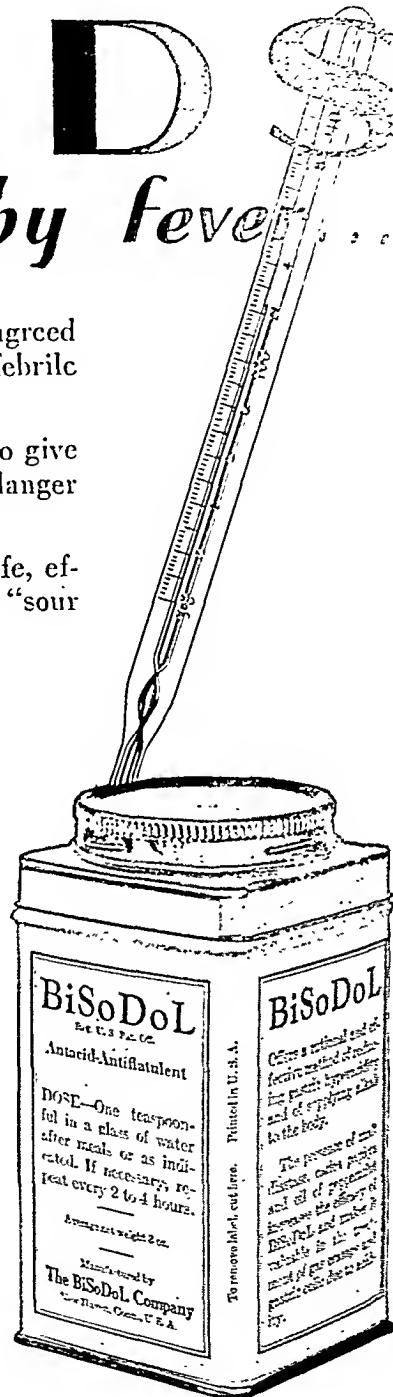
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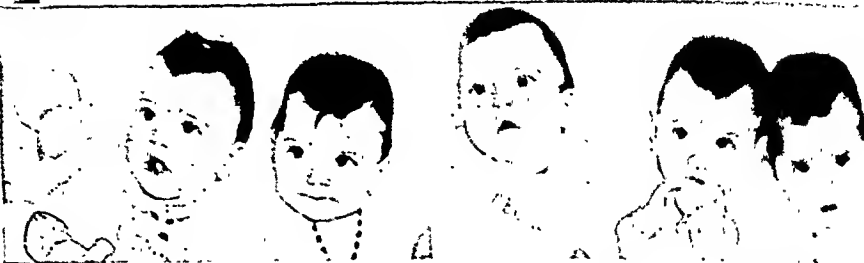
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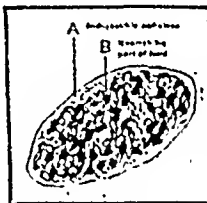
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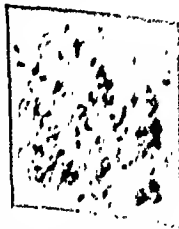
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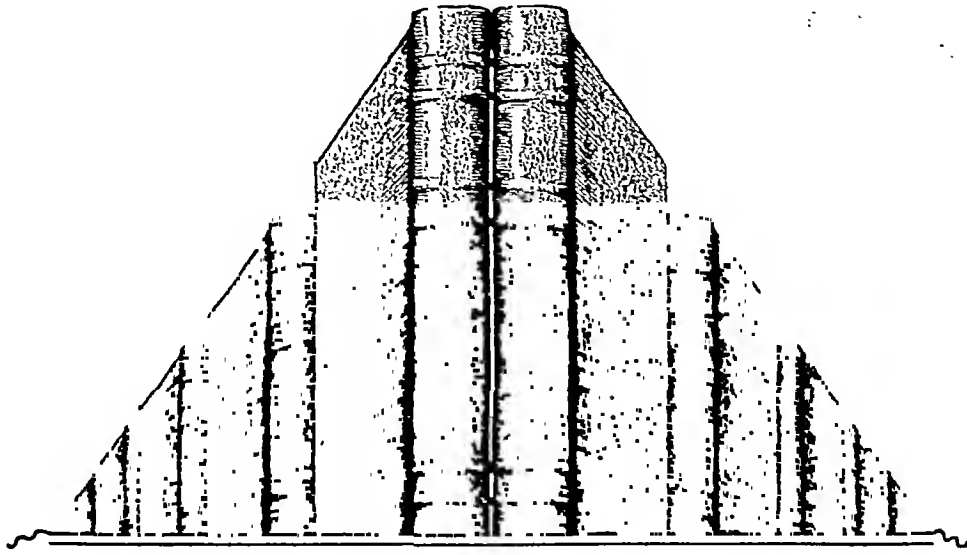
- 1 Peas, beets, asparagus tips
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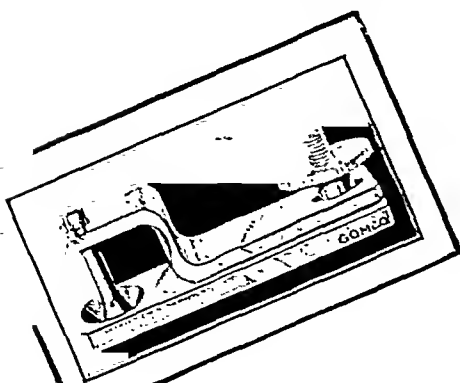
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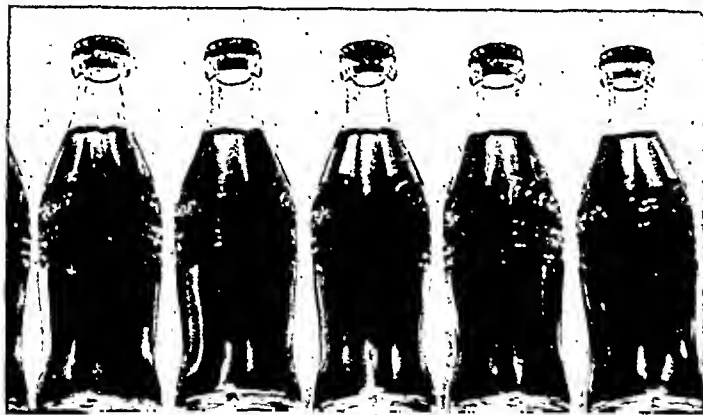
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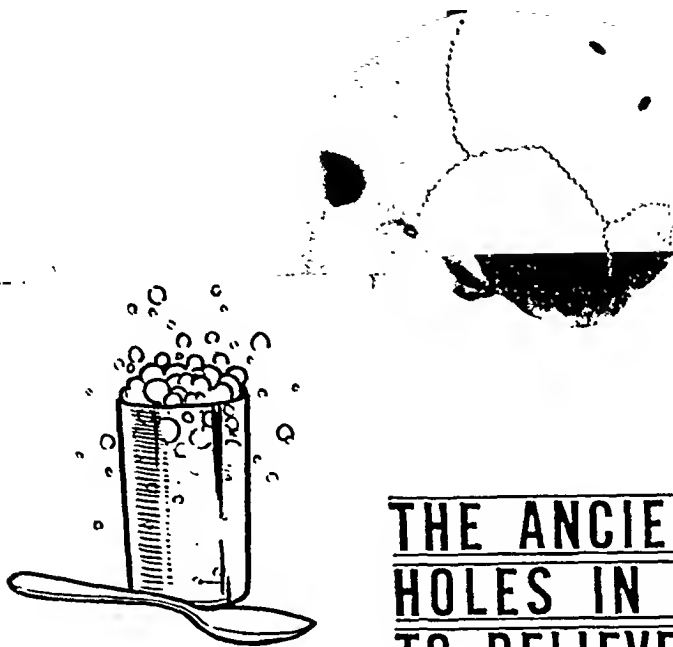
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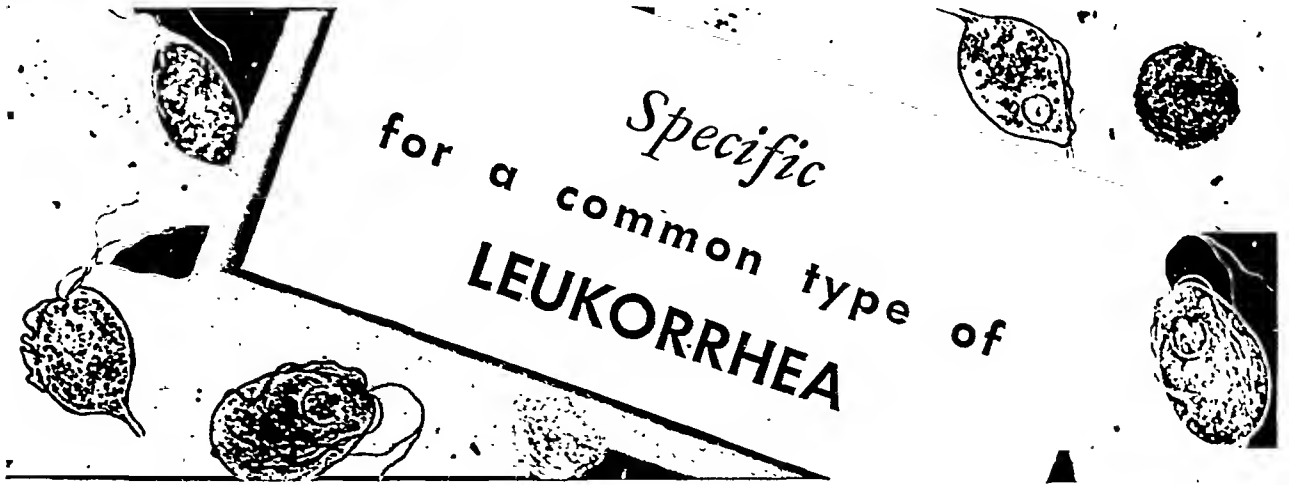
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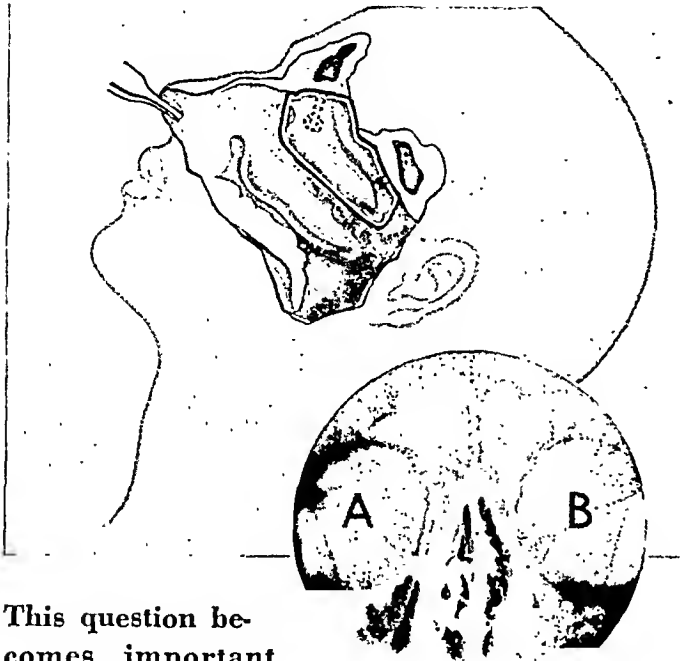
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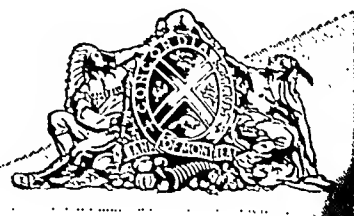
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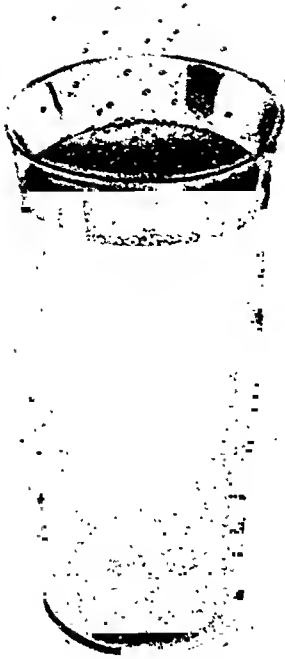
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ACIDOSIS

—IT NEED NOT BE

Acidosis is a frequent complication of febrile disease and of metabolic disorders. It tends to aggravate the disease, it probably prolongs it, eases the way to complications and sequelae, and retards convalescence. The untoward influences of acidosis can be curbed by

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ALKA ZANE



Deodorant



Lavoris corrects offensive breath chemically and mechanically. It does not disguise disagreeable odors by an aromatic flavor. It attacks the products of decay and putrefaction at their source, converts them into inoffensive compounds and eliminates them thoroughly.

Lavoris is pleasant to use. Young and old find it inviting and refreshing. This quality encourages mouth hygiene and facilitates the patient's co-operation.

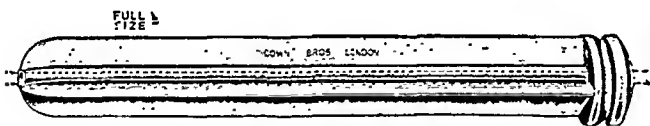
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CANADA

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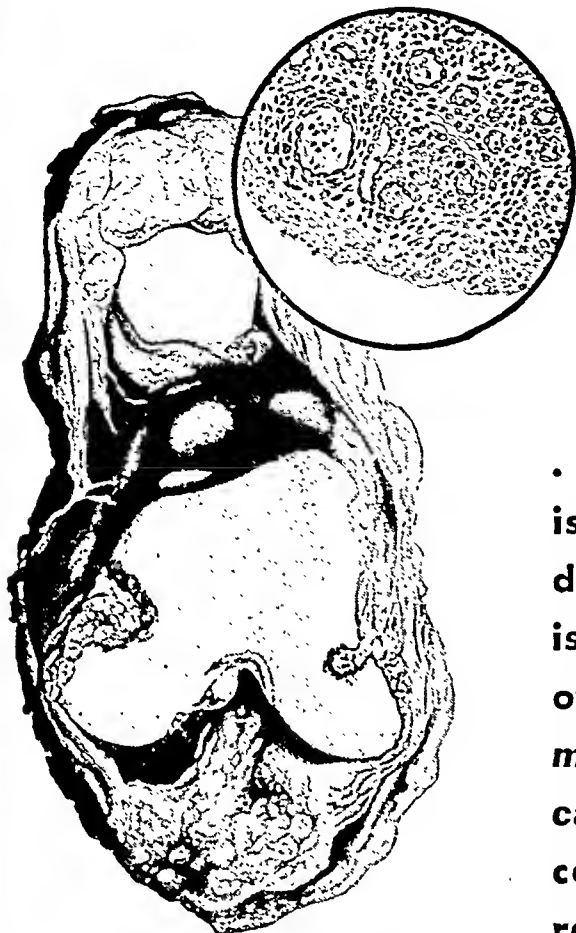
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. . . whether the cause is traumatic and the condition an acute one, or it is a painful exacerbation of chronic arthritis, the *marked stimulation to capillary circulation and cellular activity*, which results from the use of

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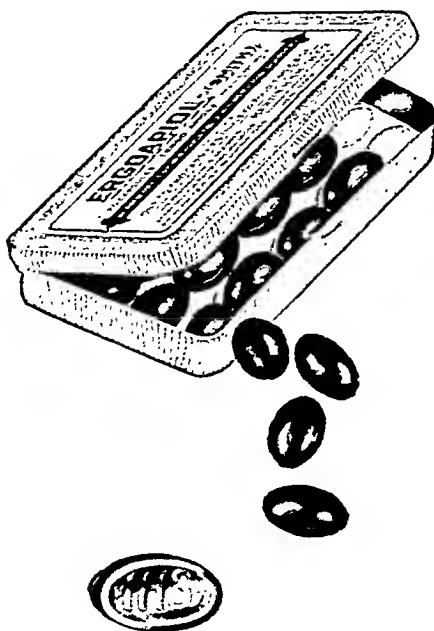
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Four years ago we published the advertisement reproduced at the left. We acknowledged the tribute willingly given by members of the profession who used Lactogen successfully in the feeding of their own infant children and grandchildren.

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A GOOD PRESCRIPTION

Physicians throughout the world prescribe ERGOAPIOL (Smith) in the treatment of *Amenorrhea*, *Dysmenorrhea*, *Menorrhagia* and *Metrorrhagia*.

ERGOAPIOL provides symptomatic benefit by stabilizing uterine tone, regulating innervation and controlling bleeding when present. By its corrective action on perverted menstrual function, it simplifies local gynecological treatment. Valuable in obstetrics during the third stage.

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DOSAGE: One to two capsules three or four times a day, preferably after meals with a glass of milk or water.

Supplied only in packages of twenty each.

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EFEDRON (HART)

For Relief of Nasal Congestion



The original water soluble Ephedrine Nasal Jelly.

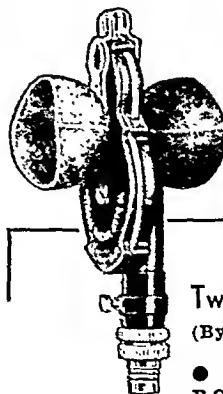
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Please send me complimentary tube EFEDRON (Hart) for clinical trial.

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Complete elimination—
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This case study tells more about Mazon than any statement we could make.



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3 simple instructions to follow . . .

1. Cleanse with Mazon Soap.
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**A distinct departure from other local treatments.



- Readily Absorbed
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- Anti-pruritic
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MAZON SOAP

guarantees best possible results from Mazon treatment. It cleanses and properly prepares the skin for the absorption of Mazon.

DO NOT ACCEPT SUBSTITUTES. Insist that your patient receive the original 1, 1½ or 4 oz. jar.

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*because of distinctive
alkalizing features...*

IN POWDER FORM

"Why don't you dispense Entacarb as a powder, too?" asked many physicians who had used Entacarb Tablets successfully since their introduction several years ago. So here it is,—a combination of the best known alkaline drugs. You will find the Powder a dependable weapon against gastric hyperacidity.

Both forms of Entacarb, and all other R. & C. products, are known only to physicians and intended exclusively for their prescriptions.



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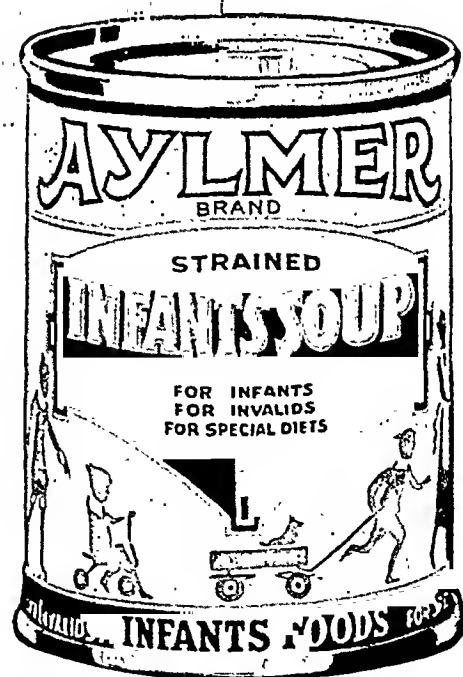
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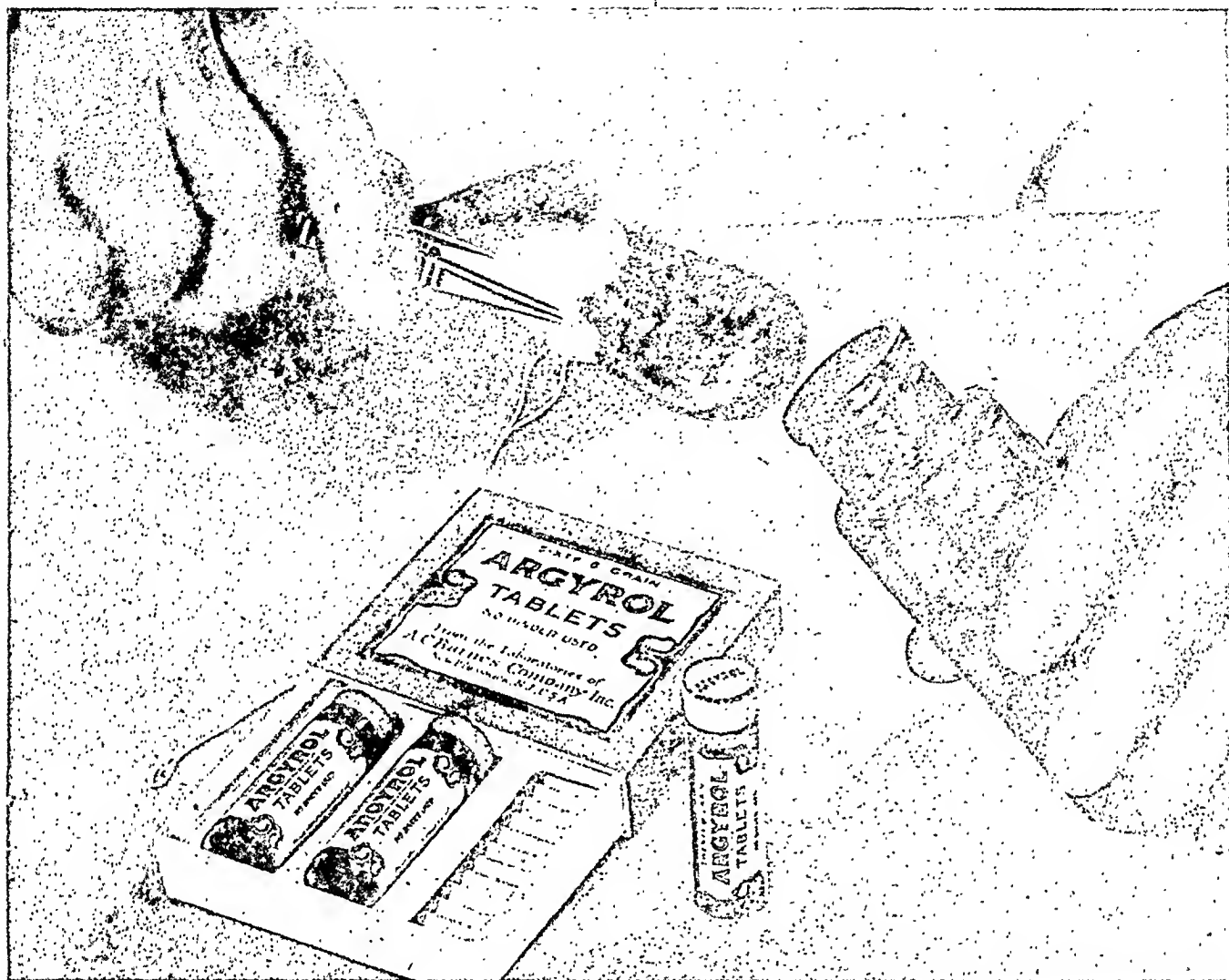
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Protect Mother and Infant with Argyrol

The best opinion of today is that antenatal treatment of all gravidae should include a thorough search for gonorrhea, irrespective of social status.

Where there is the slightest suspicion of gonorrhea in one parent or both, protection is afforded by the use of vaginal tampons saturated in 25 per cent solution of Argyrol—the standard in gonorrhea.

Argyrol's peculiarly sedative, inflammation allaying qualities, and its clinical successes of 30 years' duration may be easily accounted for by pertinent

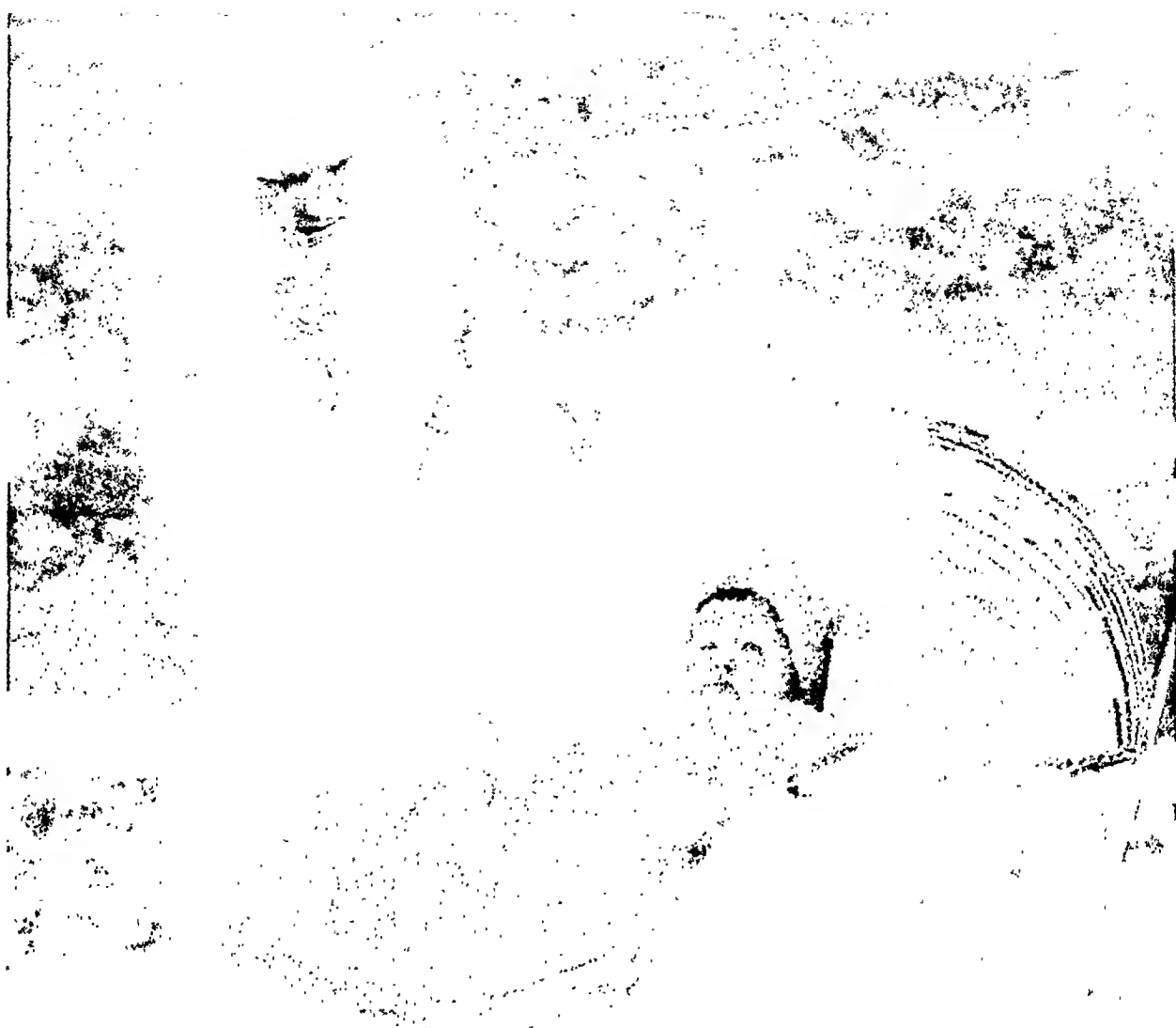
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The Canadian Medical Association Journal



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June 22-26, 1936
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THE CANADIAN MEDICAL ASSOCIATION
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